A COMPARATIVE STUDY OF GLOMERULAR FILTRATION RATE CALCULATION BY COCKCROFT-GAULT, MDRD, CKD-EPI FORMULA AND DTPA RENAL SCAN AMONG LIVE RELATED KIDNEY DONORS

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CERTIFICATE

This is to certify that this dissertation entitled **"A COMPARATIVE STUDY OF GLOMERULAR FILTRATION RATE CALCULATION BY COCKCROFT-GAULT, MDRD, CKD-EPI FORMULA AND DTPA RENAL SCAN AMONG LIVE RELATED KIDNEY DONORS"** submitted by **Dr. K. SENTHAMIZH SELVAN** to The Tamil Nadu Dr.MGR Medical University is in partial fulfillment of the requirement for the award of **M.D.DEGREE (BRANCH-1) in GENERAL MEDICINE** and is a bonafide research work carried out by him under direct supervision and guidance.

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DECLARATION

I solemnly declare that the dissertation entitled **"A COMPARATIVE STUDY OF GLOMERULAR FILTRATION RATE CALCULATION BY COCKCROFT- GAULT, MDRD, CKD-EPI FORMULA AND DTPA RENAL SCAN AMONG LIVE RELATED KIDNEY DONORS"** was done by me at Government Stanley Hospital, Department of Nephrology during 2009-2012 under the guidance and supervision of my unit Chief **Dr. G. SUNDARAMURTHY, M.D.** The dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of **M.D. DEGREE (BRANCH-I) in General Medicine.**

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CONTENTS

ABBREVIATIONS

GFR	-Glomerular filtration rate
C-G	-Cockcroft-Gault
MDRD	-Modification of Diet in Renal Disease
CKD	-Chronic kidney disease
AKI	-Acute kidney injury
CKD-EPI	-Chronic kidney disease – epidemiology collaboration
CrCL	-Creatinine clearance
DTPA	-Diethylene triamine pentaacetic acid
EDTA	-Ethylene diamino tetra-acetic acid
e GFR	-Estimated GFR
ESRD	-End stage renal disease
CVD	-Cardio vascular disease
Tc 99	-Technetium 99
K/DOQI	- Kidney disease outcome quality initiative

INTRODUCTION

CKD progresses into end stage renal disease (ESRD) inspite of our strategies to slow the progression of the disease .ESRD occurs when kidney function is not able to cope up with the body's excretory load and hemodialysis, peritoneal dialysis ,or kidney transplantation has to be substituted for native kidney function. Among them, kidney transplantation by far imparts a better quality of life in ESRD patients.

The shortage of donor organs is a global issue, that restrict kidney transplantation. Hence patients and transplant surgeons are increasingly dependent on live kidney donors. Although kidney transplantation offers a favourable outcome for the recipient, it may be associated with some risk for the donor. To minimize the risks a strict pre-operative donor evaluation is essential.

Renal function assessment of the donor is the most important part of donor evaluation. Glomerular filtration rate (GFR) is considered to be optimal test for overall assessment of renal function but serum creatinine is not considered as appropriate and only measurement of renal function, especially for detection ofearly stages of CKD due to its tubular secretion[1] and also its variability with body mass , age, sex and race.

It is well known that GFR can be precisely measured by specific filtration markers such as Inulin,I125 Iothalamate,Cr 51 EDTA,Tc99-diethylene triamino penta acetic acid (DTPA).These standard methods cannot be used in daily clinical practice unfortunately as they are expensive, time consuming and cumbersome and require specialized equipments and skills.

So a non invasive and accurate estimation of GFR is the need of the hour in Nephrology. Here comes the GFR prediction equations which are easy to apply, cost effective and less cumbersome. The new K/DOQI Guidelines also recommend estimating GFR by MDRD and COCKCROFT-GAULT equations.[2]

Hence, it sounds worthy for me to take up this comparative study of GFR calculation by COCKCROFT-GAULT formula, MDRD formula, CKD-EPI formula and DTPA renal scan among live related kidney donors .

AIMS AND OBJECTIVES

1) To estimate GFR by 3 different methods namely COCKCROFT-GAULT formula,MDRD formula and CKD-EPI formula ,among live related kidney donors .
2) To analyse how closely the GFR calculated by these formulae correlate with that of DTPA renal scan in them.

REVIEW OF LITERATURE

RENAL PHYSIOLOGY:

Glomerular filtration rate (GFR) is a product of average filtration rate of each single nephron, the filtering unit of the kidneys, multiplied by number of nephrons in both kidneys [1].It is the volume of fluid filtered from renal glomerular capillaries into Bowman's capsule per unit time. The normal level for GFR is approximately 130ml/min per 1.73m^2 for men and 120ml/min per 1.73m^2 for women. This varies according to age, sex, body size, physical activity, diet, pregnancy[5] and drug intake.GFR is usually expressed per 1.73m^2 for standardization.

GFR is 8% higher in young men than in women.GFR has a diurnal variation of 10% lower value at midnight. During pregnancy GFR increases by 50% in first trimester and values normalizes after delivery.GFR falls gradually by 0.75ml/min/year after the age of 40 years. A fall in GFR can be due to a decline in nephron number or a decline in single nephron GFR, but an increase in GFR can be due to increase in single nephron GFR or glomerular hypertrophy. Hence the level of GFR do not indicate loss of nephrons and GFR may remain within normal range inspite of substantial kidney damage.

GFR is calculated by using any chemical that has a steady level in the blood and is freely filtered but neither reabsorbed nor secreted by the

kidneys. The rate hence measured is the quantity of the substance in urine that originated from a calculated volume of blood[3].

The product of urine concentration and urine flow equals the mass of a substance excreted during the time that urine has been collected. This mass equals the mass filtered at the gomerulus as nothing is added or re-absorbed in nephron. When we divide this mass by plasma concentration we get the volume of plasma from which the mass must have come from; and thus it gives volume of plasma fluid that has entered the Bowman's capsule within that time period of time.

GFR = (urine concentration × urine flow) / plasma concentration

GFR is recorded in units of volume /time.

MEASUREMENT OF GFR :

GFR cannot be measured directly, in clinical settings it is measured as urinary clearance of an ideal filtration marker.

THE CONCEPT OF CLEARANCE :

Clearance of a substance is defined as the volume of plasma cleared of a marker by excretion per unit of time [1]. It is a measure of the renal excretion ability. Each substance has a specific clearance that depends on its filtration characteristics. Clearance is a function of glomerular filtration,

secretion from the peritubular capillaries to the nephron, and reabsorption from the nephron back to the peritubular capillaries. It doesnot represent an actual volume of plasma but a virtual volume of plasma that is completely cleared of the substance per unit of time. If the rate of elimination of a substance is high its clearance is also high. Clearance of a substance is the sum of urinary and extra renal clearance. It has units of Volume /time.

URINARY CLEARANCE:

Urinary clearance of a substance x , (c_x) is defined as:

$$C_X=(U_X \times V)/P_X$$

Where U_X -Urinary concentration; P_X -plasma concentration; V-Urine flow rate

An ideal filtration marker is one which is filtered freely, not secreted and not reabsorbed. If a substance is filtered and secreted ,urinary clearance is greater than GFR and if a substance is filtered and reabsorbed urinary clearance is lesser than GFR.

PLASMA CLEARANCE:

Plasma clearance of a substance x, ($C_{X)}$ is defined as

$$\mathbf{C_X = A_X / Px}$$

Where A_X is amount of marker administered and P_X is plasma concentration . Plasma clearance of a substance also depends on filtration, tubular secretion, and tubular re-absorption and in addition extra renal elimination.

PRESSURE DEFINITION OF GFR:[4]

GFR is the fluid flow rate between glomerular capillaries and bowmans capsule

$$dq/dt = Kf \times (Pg - Pb - \pi g + \pi b)$$

dq/dt is the GFR

Kf is the filtration constant and is defined as product of hydraulic conductivity and surface area of glomerular capillaries

Pg is the hydrostatic pressure within the glomerular capillaries

Pb is the hydrostatic pressure within bowmans capsule

Πg is colloid osmotic pressure within glomerular capillaries

Πb is colloid osmotic pressure within bowmans capsule

MEASUREMENT OF RENAL PLASMA FLOW:

The use of the clearance technique and the availability of substances that undergo both glomerular filtration and tubular secretion have made it

possible to measure renal plasma flow (RPF). Paraamino hippuric acid (PAH) is an organic acid that is filtered by the glomerulus and actively secreted by the proximal tubule. The amount that is found in the final urine is the sum of the PAH filtered plus the component that is secreted.When the plasma concentration of PAH is lower than 10mg/dl, most of the PAH reaching the peri-tubular capillaries is cleared by tubular secretion and little PAH appears in renal venous plasma. Under these circumstances, the amount of PAH transferred from the plasma to the tubular lumen via filtration and secretion approximates the amount of PAH delivered to the kidneys in the plasma .

Therefore,

RPF = (Upah × V) / Ppah

Where Upah and Ppah are the concentrations of PAH in the urine and plasma, respectively and V is the urine flow rate.

Renal blood flow (RBF) = (RPF / 100-Hematocrit) × 100

The most important limitation of this method is the renal extraction of PAH. The latter is always less than 100%. At high plasma concentrations, fractional tubular secretions of PAH declines and significant amount appear in the renal veins, under these circumstances, PAH clearance seriously under estimates RPF.

AUTO REGULATION OF RENAL BLOOD FLOW AND GFR:

Acute variations in arterial blood pressure inevitably cause corresponding changes in RBF and GFR, these changes are short lived and provided the blood pressure remains within the normal range, compensatory mechanisms come into play after a few seconds to return both RBF and GFR to near normal. This phenomenon is called auto-regulation .This is brought about by two different mechanisms:

1) A myogenic reflex, whereby the afferent arteriolar smooth muscle wall constricts automatically when renal perfusion rises.
2) Tubulo-glomerular feedback, whereby an increased delivery of Nacl to the macula densa region of nephron, resulting from increases in blood pressure RBF, and GFR, vasoconstriction of the afferent arteriole supplying that nephron's glomerulus

These mechanisms restores both RBF and glomerular capillary pressure towards normal, the initial change in GFR is also reversed. But these auto regulatory mechanisms operate only within a mean arterial pressure range of 80 to 180 mmHg.

MEASUREMENT OF GFR USING EXOGENOUS FILTRATION MARKERS :

Inulin is polymer of fructose, historically described as the ideal filtration marker and was considered gold standard method in the past. GFR can be determined by injecting Inulin into plasma, allowed to achieve a steady state concentration and bladder is catheterised for strict urine collection. Since Inulin is neither reabsorbed nor secreted by kidney after glomerular filtration, its rate of excretion is directly proportional to the rate of water and solutes across glomerular filter. This method is cumbersome and not commonly used. Inulin clearance slightly overestimates GFR. In early stages of renal disease the inulin clearance may remain normal due to hyperfiltration in remaining nephrons. Due to these drawbacks alternative exogenous markers like iothalamate, iohexol, DTPA are used now.

ENDOGENOUS FILTRATION MARKERS:

Creatinine is frequently used endogenous filtration marker, urea and now cystatin–C are also used. The plasma level of a marker is related to the reciprocal of the level of GFR, but it is also influenced by eneration, tubular secretion, re-absorption and extra renal elimination collectively called as non-GFR determinants of the plasma level. In a steady state, a constant plasma level is maintained .

CREATININE BASED GFR MEASUREMENT:

Creatinine is produced naturally by the body. It is a break down product of Creatine phosphate, which is found in muscle. Other sources are dietary meat intake, or creatine supplements. Its production depends on muscle mass. It is freely filtered by the glomerulus, but actively secreted by the peritubular capillaries. Several medications inhibit this secretion and hence raising creatinine level. Creatinine in intestinal secretion is degraded by bacteria, leading to low levels. In case of low GFR this extra renal excretion of creatinine is increased. Unlike precise GFR measurement involving constant infusion of inulin, creatinine is already at a steady state concentration in the blood and so measuring creatinine clearance is much less cumbersome .

However, creatinine estimates of GFR have their limitations. All of the estimating equations depend on a prediction of 24 hr creatinine excretion rate, which is a function of muscle mass. One of the equation COCKCROFT-GAULT do not correct for race.

Creatinine synthesis depends on muscle mass. Cachectic patients and cirrhotic patients have low net muscle mass and lower creatinine excretion rate than predicted by equations. Hence a creatinine value of 1 mg/dl may appear normal but actually these patients may have renal failure. Similarly creatinine value of 1.5 may be normal in a obese individual

CREATININE CLEARANCE (C Cr) :

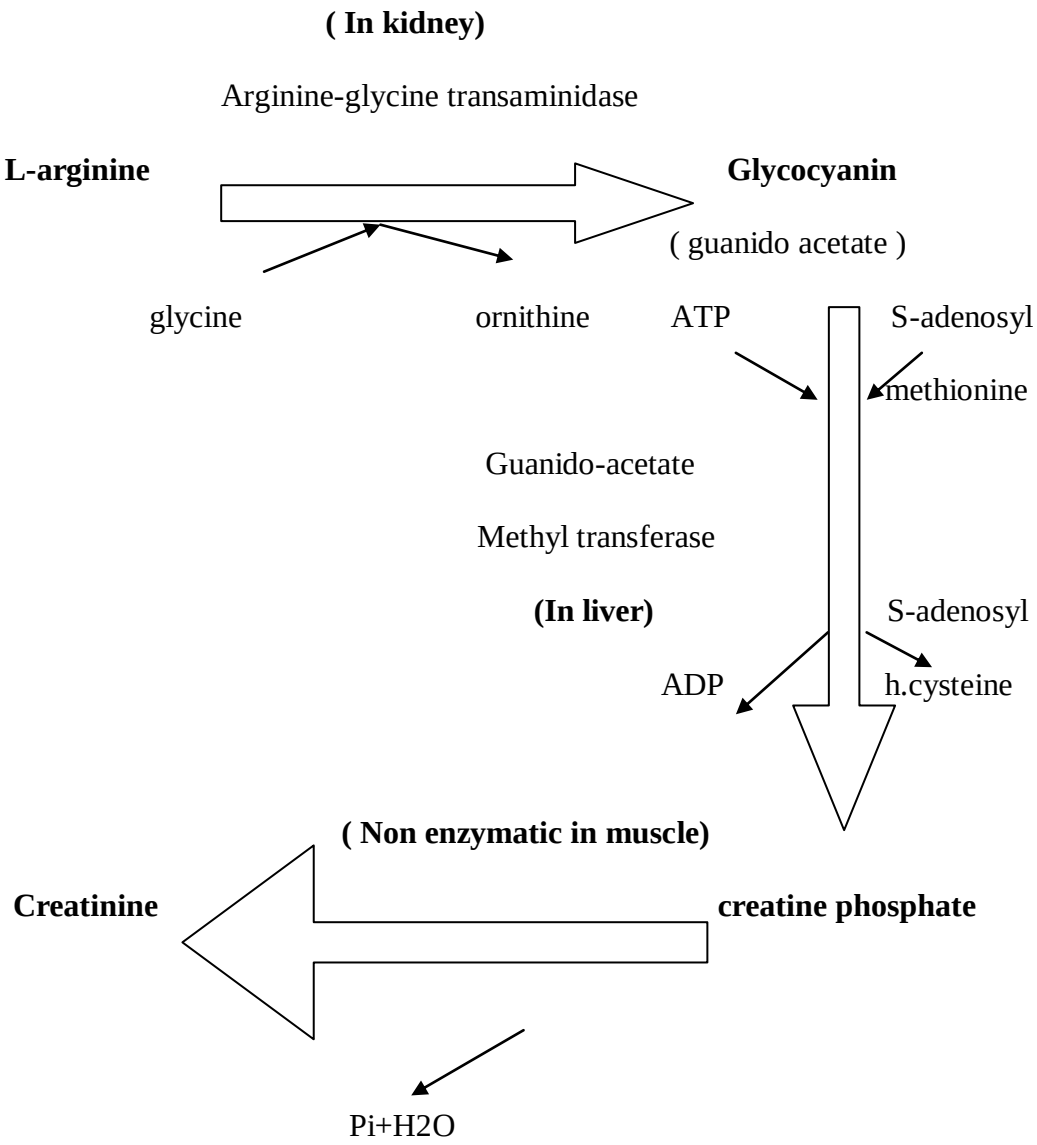
Creatinine clearance is calculated from creatinine concentration in collected urine sample (UCr), urine flow rate (V) and creatinine concentration in plasma (P Cr)

$$\mathbf{C\ Cr = (U\ Cr \times V) / P\ Cr}$$

However creatinine clearance is not widely measured anymore due to

1) Difficulty in assuring a complete urine collection
2) Variability due to muscle mass, age, race, sex

BIOSYNTHESIS AND METABOLISM OF CREATININE [6]



FACTORS AFFECTING SERUM CREATININE CONCENTRATION[7]

PARAMETERS	EFFECT ON S.CREATININE	MECHANISM
Age	Decreases	Decreased creatinine production due to age related reduction in muscle mass
Female sex	Decreases	Decreased creatinine production due to age related reduction in muscle mass
African American race	Increases	Increased creatinine production due to high muscle mass
Vegetarian diet	Decreases	Decreased creatinine production
Dietarymeat,creatine supplements	Increases	Transient increase in creatinine generation
Muscular individuals	Increases	Increased generation of creatinine and increased muscle protein
Obesity	No change	Excess mass is only fat
Trimethoprim, Cimetidine,fibrates	Increases	Reduced tubular secretion of creatinine
Ketoacids, Cephalosporins	Increases	Interference withalkaline picrate assay for creatinine.

CREATININE ASSAY:

In Jaffe's assay (alkaline picrate assay) chromogens are generated depending upon concentration of creatinine. Here main drawback is chromogens other than creatinine gives a false positive values.Modern enzymatic assays do not detect other chromogens. Due to heterogeneity in creatinine assays, global standardization of creatinine assays has to be enforced strictly.[8] In Ross et al study[9], the average coefficient of variation serum creatinine in laboratories was 8% and 13% overestimation of values when compared to reference standard.

ESTIMATED GFR USING COCKCROFT-GAULT FORMULA:

$$\text{Crcl} = \frac{(140 - Age) \times (Weight\ in\ kg)}{(Serum\ creatinine)(72)} \times (0.85\ if\ female)$$

Thus estimated Creatinine clearance using Cockcroft-gault formula depends on age, body weight, Sex[10]. As age increases creatinine clearance decreases, and women have 15% lower creatinine clearance than men of same age and body weight.

Limitations of this equation are :

-it is not accurate in cases where GFR is > 60ml/min

-it overestimates GFR

-it was derived by older creatinine assay methods

-drug dosing by this method is inaccurate , (Stevens et al [11])

ESTIMATED GFR USING MDRD FORMULA:

$$= 186 \times (SCR)^{-1.154} \times (age)^{-0.203} \times$$
$$(0.742\ if\ female) \times (1.210\ african\ american)$$

MDRD (Modification of diet renal disease) formula (6 variable) was initially introduced, with following parameters: age, race, sex, serum creatinine, blood urea, serum albumin. This formula was revised and reintroduced, MDRD (4 variable). Here the parameters are age, race, sex, serum creatinine.[12]

Advantages of 4 variable MDRD over 6 variable MDRD are that it is better validated in diabetic kidney disease, kidney transplant recipients and in African-Americans. MDRD formula underestimates GFR in patients with GFR more than 60.The utility of MDRD formula has not been validated in children, in patients with serious co-morbid conditions, in healthy persons, or in individuals older than 70 years of age. It is also not validated in an acute kidney injury setting. Inspite of that, it is recommended for clinical assessment of kidney function[13]. Morethan 70% of labs in USA follows MDRD (American college of pathologists) [14].Also MDRD is increasingly being used in all races and ethnic groups[15]. In

august 2005 the Australasian creatinine consensus working group recommended that whenever serum creatinine estimation is requested GFR using MDRD may be given along with it, in patients aged over 18 years.[24]

ESTIMATED GFR USING CKD-EPI FORMULA:

$$=141 \times \min(SCr/k,1)^{a} \times \max(SCr/k,1)^{-1.209} \times 0.993^{age} \times [1.018 \text{ if female}] \times [1.159 \text{ if black}]$$

where SCr is serum creatinine (mg/dL), k is 0.7 for females and 0.9 for males, a is -0.329 for females and -0.411 for males, min indicates the minimum of SCr/k or 1, and max indicates the maximum of SCr/k or 1.

The CKD-EPI (chronic kidney disease epidemiology collaboration) formula was published recently in may 2009. It was developed in an effort to create a formula more accurate than the MDRD formula, especially when actual GFR is more than 60ml /1.73m2. Researchers pooled data from multiple studies, diverse clinical populations, to validate this new equation[16]. The CKD-EPI equation performed better than MDRD equation, with less bias and greater accuracy. It also resulted in restaging of the CKD patients who were staged according to the MDRD formula[23]. After introduction of CKD-EPI, now GFR is reported for all ranges of the kidney function and CKD-EPI should replace MDRD equation for routine clinical use [John Feehaly].

ESTIMATION OF GFR BY OTHER ENDOGENOUS MARKERS:

UREA:

It is an end product of protein catabolism by the liver. It is freely filtered by the glomerulus and passively reabsorbed in tubules. Hence it underestimates GFR. In cases of reduced renal perfusion due to volume depletion or anti-diuresis urea absorption is further increased thereby lowering GFR further. Urea generation is increased in cases of catabolic states like infection, chemotherapy, hyper-alimentation or GI bleed. Urea generation is decreased in liver disease and severe malnutrition.

CYSTATIN–C:

Cystatin-c is a protein with a molecular mass of 13kd. It has following functions[17]

-inhibiton of cysteine protease

-anti-bacteial and anti-viral action

-immuno modulatory effects

-modulation of body response to brain injury.

Cystatin-C is produced by all nucleated cells at a constant rate. It is freely filtered, and 99% is reabsorbed and catabolised only 1% remaining is excreted though some element of tubular secretion and extra renal elimination is also found out in some studies[17],[18].

Cystatin –C levels were found to be high (after correcting for measured GFR) due to following factors: male sex, old age, whites, obesity, hypoalbuminemia and diabetes [21],[22]

Assays for cystatin-C are expensive . Two methods used are:

1) particle enhanced turbidimetric assays

2) particle enhanced nephelometric assays

Cystatin –C levels in serum predicts GFR better than creatinine but equations in based on cystatin –C are not considered better than creatinine based equations. In cases of acute kidney injury serum cystatin –C was found to be an earlier when compared to creatinine[19].There are some studies which show that equations employing both creatinine and cystatin-C are better predictors of GFR[20],[25]. Cystatin –C was found to be better marker in diabetic patients when compared to creatinine [26]

DTPA RENAL SCAN:

The nuclear medicine renal scan is commonly performed by using DTPA

(Diethylene triamine penta acetic acid) radio labeled with Technetium 99. Its clinical implications are to evaluate:

1) the blood supply of the kidneys

2) the function and excretion of urine from the kidneys

3) split GFR of each kidneys

4) renal tubular function and perfusion

5) reno-vascular hypertension

6) renal artery stenosis

7) renal tubular obstruction and trauma or damage

8) blockage or interruption of the ureters

9) renal transplant perfusion and function

PREPARATION OF THE PATIENT:

First of all the patient has to be hydrated adequately. In case of reno-vascular hypertension or suspected renal artery stenosis, anti-hypertensives have to be stopped 4-7 days prior to the examination. In case of pregnancy and breast feeding precautions has to be taken to stop breast feeding and minimize non- essential contact with the baby for a short period of time .

For the DTPA renal scan patient has to lie supine on the scanning bed, with the gamma camera under the bed. The patient should not move during scanning as it will blur the images and give poor scan results. An IV cannula is placed, radiolabelled DTPA is injected and this can be detected by the gamma camera .

After 15 minutes of scanning IV frusemide injection is given, this helps by

1) Increasing the amount of urine that the kidney makes, by decreasing amount of water that the kidney reabsorbs.
2) Increasing flow of urine in the tubules and the ureter thereby enabling tubular details.

After 30 minutes of scanning ask the patient to void urine, once the bladder is emptied, scanning is continued for further 2 minutes, and a repeat scanning is done at 4 hours. The IV cannula is removed after the procedure .There are no after effects of a DTPA renal scan.

IMPLICATIONS OF ESTIMATED GFR:

IN CHRONIC KIDNEY DISEASE-

Recent guidelines states early detection of CKD by monitoring for albuminuria or measuring GFR, and serum creatinine is a poor marker for early CKD. Our estimating equations based on creatinine are found to be less accurate when due to multiple factors affecting measured creatinine values. Hence exogenous filtration markers or timed urine collection for creatinine clearance are to be employed in future

IN ACUTE KIDNEY INJURY-

AKI is a non–steady state. The endogenous filtration markers requires time for retention before their levels raise in blood. During

recovery from an AKI, even after normalization of GFR, the filtration markers may take time for their clearance. Hence estimated GFR values may not reflect the actual measured. In those cases only a change in estimated GFR may reflect the magnitude and direction of the change in measured GFR.

CHRONIC KIDNEY DISEASE (CKD)

DEFINITION:

CKD is defined as

1) Kidney damage for 3 months or longer, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR), manifesting by either :
    A) Pathological abnormalities
    B) Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging
2) GFR of less than 60 ml/min per 1.73m^2 for more than 3 months with or without kidney damage.

In other words CKD is defined by the presence of sustained abnormalities of the renal function and results from various causes of renal injury. CKD can lead to progressive loss of renal

function, and may terminate in ESRD after a variable period of time following the initiation injury. There has been lot of changes in the collective view of CKD. The terms chronic renal insufficiency, chronic renal failure, chronic renal disease have all been replaced by the single term chronic kidney disease

STAGES OF CKD:

NKF-K/DOQI[2] CKD staging

STAGE	DESCRIPTION	GFR,ml/min/1.73m^2
-	At increased risk	>60 with CKD risk factors
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with slightly decresased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney failure	<15

The risk factors for CKD include hypertension, diabetes mellitus, autoimmune disease, older age, African ancestry, family history of renal disease, a previous episode of acute renal failure, abnormal urinary sediment, structural abnormalities of the urinary tract. and the presence of proteinuria (micro-albuminuria or overt proteinuria)

STAGING RENAL INVOLVEMENT BASED ON PROTEINURIA

Stage	Urine dipstick test for protein	24hr urine albumin
Normal	Negative	< 30mg/day
Microalbuminuria	Negative	30-300 mg/day
Macroalbuminuria (overt proteinuria)	Positive	>300 mg/day

PATHOPHYSIOLOGY OF CKD:

Two sets of mechanisms operate, to produce renal disease

1) Initiation of renal injury by immune complexes, chemical mediators of inflammation or toxins.

2) Progression of renal injury by mechanisms like hyperfiltration and hypertrophy of the remaining nephrons.

Glomerular hyper filtration can maintain GFR initially, but later can lead to glomerular injury. Abnormal glomerular permeability can initiate proteinuria thereby aggravates glomerular injury. There are also evidences to suggest that proteinuria can cause tubulointerstitial disease. The extent of tubulointestitial damage determines renal disease progression in all forms of glomerular disease.

RISK FACTORS FOR PROGRESSION OF CKD

1) Ethnicity is a risk factor for many renal diseases. African American diabetics have three fold higher risk of developing ESRD. They also develop HIV-associated nephropathy more frequently than the rest.
2) Gender is an additional risk factor for renal disease progression as the overall incidence of ESRD is greater in males than in females .
3) Smoking is associated with kidney disease progression in diabetes, IgA nephropathy, lupus nephritis, and polycystic kidney disease

4) Increased consumption of non narcotic analgesics has been associated with increased risk of CKD.

MEASURES TO RETARD PROGRESSION OF RENAL DISEASE :

Optimal control of BP is very important to retard the progression of renal disease. The joint national committee (JNC) -7 recommends BP reduction to below 130/80mm Hg in case of diabetics and CKD patients. Inhibition of the Renin-Angiotensin and Aldosterone system by Angiotensin converting enzyme (ACE) inhibitors and Angiotensin receptor blockers has renoprotective effects [RENAALSTUDY, IDNT STUDY, UKPDS STUDY, HOPE STUDY, REIN STUDY]

RENAL REPLACEMENT THERAPY (RRT):

It is defined as life supporting measures employed for renal failure. It includes:

1) Hemodialysis
2) Peritoneal dialysis
3) Hemofiltration
4) Renal transplantation

CRITERIA FOR RRT:

- Creatinine clearance of <10ml/min/1.73m^2
- Hyperkalemia refractory to medical measures
- Volume over load status
- Metabolic acidosis refractory to medical measures
- Bleeding diathesis

HEMODIALYSIS:

The principle behind hemodialysis is diffusion of solutes across semi-permeable membrane. The dialysate flows opposite to blood flow direction in extra corporeal circuit, this counter-current flow maintains concentration gradient increasing efficacy of dialysis. Hemodialysis removes urea, potassium and free water from the blood.

HEMOFILTRATION:

It requires a semi-permeable membrane, and the dynamics are governed by convection rather than diffusion. Dialysate is not used here , hence a positive hydrostatic pressure is needed for driving water and solutes to filtrate compartment. This drags both small and large solute particles.This procedure causes less hemodynamic instability when compared to hemodialysis but, this is an expensive option.

PERITONEAL DIALYSIS:

Here the peritoneal membrane acts as semi-permeable membrane and the dialysis fluid is instilled in the peritoneal cavity. The solutes are removed by diffusion and excess fluid is removed by osmosis. This is a simple procedure and effective both in children and elderly

Types of peritoneal dialysis :

- Continuous ambulatory peritoneal dialysis
- Automated peritoneal dialysis
- Intermittent peritoneal dialysis
- Night intermittent peritoneal dialysis
- Tidal intermittent dialysis

RENAL TRANSPLANTATION:

It is the procedure of transplantation of kidney in a patient having end stage renal failure. Patient can gain a life expectancy of 10-15 years excess, when compared to patients placed of dialysis. Transplantation should be opted as soon as the ESRD is diagnosed, as patients placed on dialysis for longer duration before transplantation are found to have lesser survival, when compared to the earlier transplantation group.

PATIENT SELECTION

Age is usually <70 years, although patients older than 75 years showed better life expectancy after transplantation when compared to dialysis. Patients should not receive transplant in following situations-

1) Active infection
2) Ongoing active immunologic disease
3) Metastatic malignancy
4) Inability to follow drug regimen due to mental illness or any substance abuse

HIV infection was historically a contraindication to transplantation, but successful kidney transplantation is possible if they have a CD4 count of >200 cells/cumm, they are free from opportunistic infections and have negligible viral load.

INDICATIONS FOR RENAL TRANSPLANTATION:

1) End stage renal disease
2) Glomerulo nephritis
3) Polycystic kidney disease
4) Autoimmune conditions SLE
5) Malignant hypertension

CONTRAINDICATIONS FOR RENAL TRANSPLANTATION:

1) Malignancy
2) Liver disease
3) Cardio-pulmonary insufficiency
4) Substance abuse and mental illness

   Smoking and obesity are associated with increased peri-operative complications.

COMBINED KIDNEY AND PANCREAS TRANSPLANTATION:

This procedure is being tried in type-1 diabetics with diabetic nephropathy. It may be of two types

1) Combined kidney and pancreas transplant
2) Pancreas after kidney transplant

COMPLICATIONS OF RENAL TRANSPLANTATION:

1) Transplant rejection
2) Infection and sepsis due to immune suppressants
3) Post transplant lympho-proliferative disorders
4) Electrolyte imbalances
5) Acne, hirsutism, hair loss, obesity, dyslipedemia, diabetes.

FUTURISTIC APPROACH TO CKD:

The Renal Physician's association and The National Kidney Disease Education program, proposed several CKD clinical guidelines .These address bone disease, hypertension, nutrition, and cardiovascular disease. Most recently, two significant changes have occurred. First, there is a big push to make guidelines in CKD as a global perspective. Second, there is tremendous enthusiasm to raise the awareness of CKD as a public health problem both in the developed world and in the developing world.

Despite all these progresses, much remains to be done. Although strategies to slow progression are available, such as angiotensin blockade and a more aggressive target for blood pressure reduction, many patients still progress to end stage renal disease. Understanding the role of genetic factors in disease progression and in disease treatment(pharmacogenomics) remains an embryonic field as it pertains to the CKD care .

The role of much investigated measures, such as dietary protein restriction remains unresolved .Although the toll that cardiovascular disease (CVD) has taken and continues to take, in terms of morbidity and mortality in CKD patients is obvious and staggering, the precise role of factors that account for this heightened risk of CVD remains unclear. Preventing CVD in CKD patients continues to be an important challenge .

The mechanistic aspects of the complications of CKD (eg. Abnormalities in mineral metabolism and anaemia) have not been completely resolved ;nor for that matter have all aspects of treatment. For example the optimal hemoglobin target in a CKD patient remains a conjecture. The management of bone and mineral metabolism continues to be challenging. To try and improve CKD management and implement guidelines in CKD patients, the concept of CKD CLINIC has emerged.

The CKD CLINIC is a multi-disciplinary clinic led by a physician or a nurse that focuses on all aspects of CKD care, running the gamut from renal progression management to the treatment of complications. Although many centres are now setting up CKD CLINICS, the precise structure of these clinics, the target population, and the relationship between the CKD CLINIC and referring doctors has not been worked out. It is hoped that the next decade will herald new data and better evidence will allow us to tackle CKD care as a global issue.

MATERIALS AND METHODS

STUDY DESIGN : observational study

STUDY PLACE : Department of Nephrology

Government Stanley Hospital

Chennai-1

STUDY PERIOD : 6 months (april 2011-september 2011)

STUDY POPULATION: Individuals attending Nephrology OPD for

undergoing evaluation for kidney

transplantation

SAMLE SIZE : 50 individuals

SAMPLING : Simple random sampling

INCLUSION CRITERIA:

Normal individuals who are willing for kidney donation and undergoing evaluation for the same.

EXCLUSION CRITERIA:

1)Age <20 and > 55 years

2)ABO incompatibility

3)Donors with h/o HT,DM

4) Donors with newly detected HT,DM

5)Females with h/o gestational diabetes and gestational hypertension

6)Donors with family h/o renal disease

After getting approval from the institutional ethical committee the study was started, All the individuals were given information form and consent form. After signing the informed consent form they were enrolled into the study.

HOW THE STUDY WAS CONDUCTED:

Individuals who were willing for kidney donation for their relatives and friends were included . They were maintained on a regular diet, and were subjected to thorough history, clinical examination, biochemical investigations, screening ultrasonogram of the abdomen and finally DTPA renal scan.

Assessment panel includes-

- Measurement of body weight in kg
- Blood pressure
- Biochemical investigations:
    - Urine : albumin,sugar,deposits
    - Hemoglobin
    - Blood grouping and typing
    - Bleeding time and clotting time
    - Random blood sugar
    - Blood urea nitrogen
    - Serum creatinine
- Screening ultrasonogram of the abdomen

Results were duely collected and analysed.

Glomerular filtration rate was calculated by the following methods. Downloadable calculators were used for calculation.These calculators requires only the variables to be substituted.

COCKCROFT-GAULT FORMULA:

$$\text{eGFR}=\frac{(140-Age)\times Weight\ in\ kg)}{(Serum\ creatinine)(72)}\times(0.85\ if\ female)$$

MDRD FORMULA FOR e GFR :

$$186 \times (SCR)^{-1.154} \times (age)^{-0.203} \times (0.742\ if\ female) \times (1.210\ if\ African\ American)$$

CKD-EPI FORMULA FOR e GFR:

141 x min $(SCr/k,1)^{a}$ x $max(SCr/k,1)^{-1.209}$ x 0.993^{age} x [1.018 if female] x [1.159 if black]

where SCr is serum creatinine (mg/dL), k is 0.7 for females and 0.9 for males, a

is -0.329 for females and -0.411 for males, min indicates the minimum of

SCr/k or 1, and max indicates the maximum of SCr/k or 1.

Then they were subjected to the DTPA RENAL SCAN:

Preparation for DTPA SCAN :

They were given 1 litre of water to drink one hour before the procedure, patient was called again and Tc 99 labelled DTPA injection was given intravenously. Then the patient was made to lie in supine position on the table where the film was being taken from above. After injection of

the dye film was taken from zero minute to upto 30 minute. IV injection frusemide 20mg was given at 15^{th} minute. After that patient was asked to void urine and immediately a post void film was taken. Four hours later another film was taken.

No adverse reactions were observed during and after the procedure. Now the results were analysed, how closely the estimated values correlate with that of the DTPA renal scan.

Correlation was made by calculating pearson co-relation coefficient, Student `t` test was used for comparison.`R` statistics were obtained by simple linear regression. This reflects the predictive ability of the model. p-value of 0.05 was considered statistically significant. The Bland and Altman method was used to determine concordance between DTPA scan with the prediction equations.

RESULTS

This study included 50 individuals who underwent renal donor workup at the Department of Nephrology, Government Stanley Hospital. Their GFR was calculated by 3 different methods namely COCKCROFT-GAULT formula, MDRD formula and CKI-EPI formula and they were compared with the DTPA renal scan reports. The results were tabulated and analysed as follows :

Table 1 . AGE DISTRIBUTION

AGE GROUP (years)	NUMBER	PERCENTAGE
<30	7	14
31-40	11	22
41-50	19	38
>51	13	26

Table 2 .SEX DISTRIBUTION

SEX	NUMBER
Male	12
Female	38

Table 3 . SEX AND AGE GROUP DISTRIBUTION

AGE GROUP (years)	MALES		FEMALES	
	NO.	%	NO.	%
<30	1	2	6	12
31-40	4	8	7	14
41-50	3	6	16	32
>51	4	8	9	18

PARAMETERS	TOTAL	MALES	FEMALES
MEAN	43.4	43	43
MEDIAN	45	45	45
STD.DEVIATION	9.5	10	9
RANGE	31	26	31

Thus it is evident majority of our study group belongs to the age group of 41-50 years and almost three forth of our study group comprises of females.

Chart 1 . AGE DISTRIBUTION:

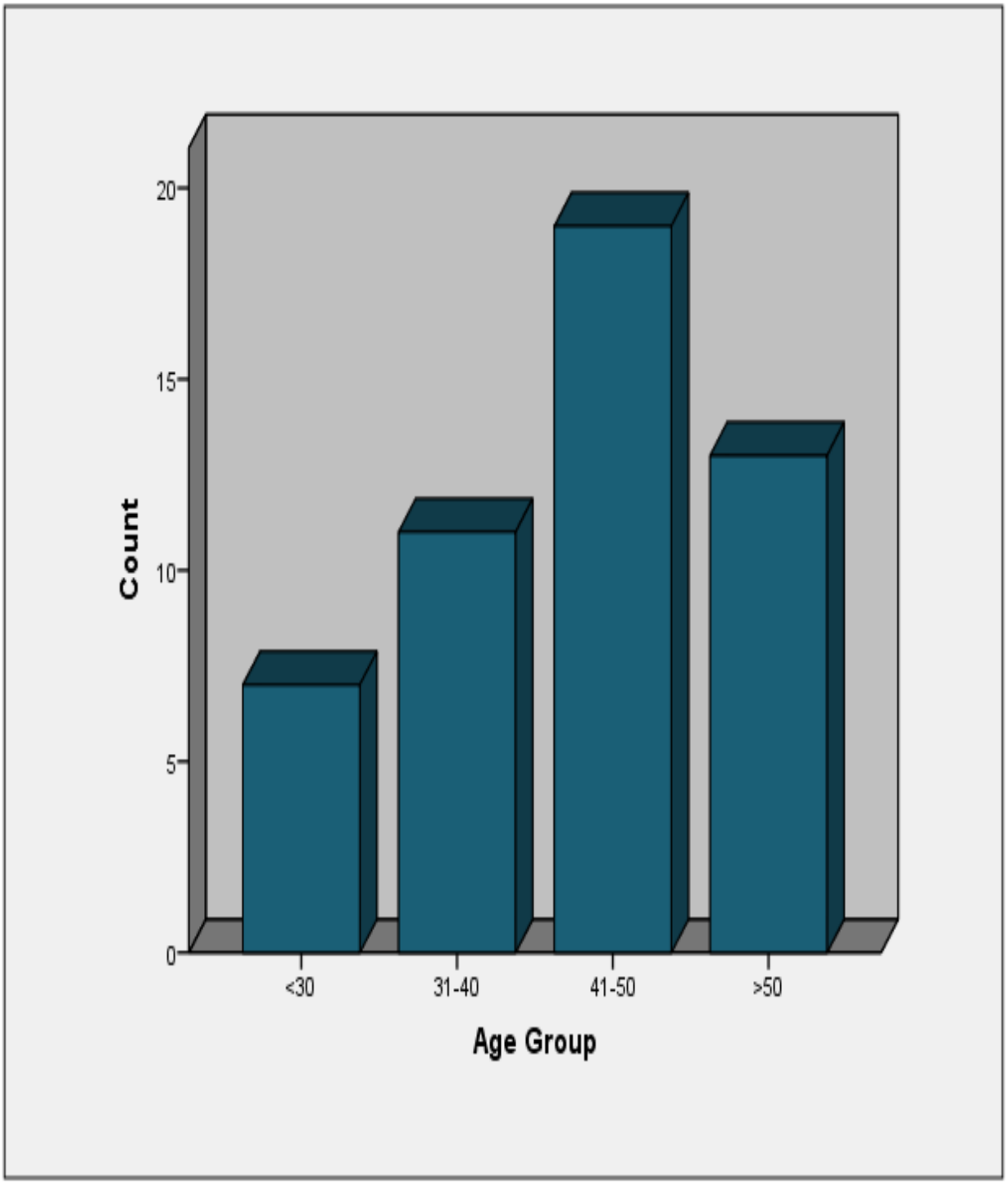


Chart 2 .**SEX DISTRIBUTION:**

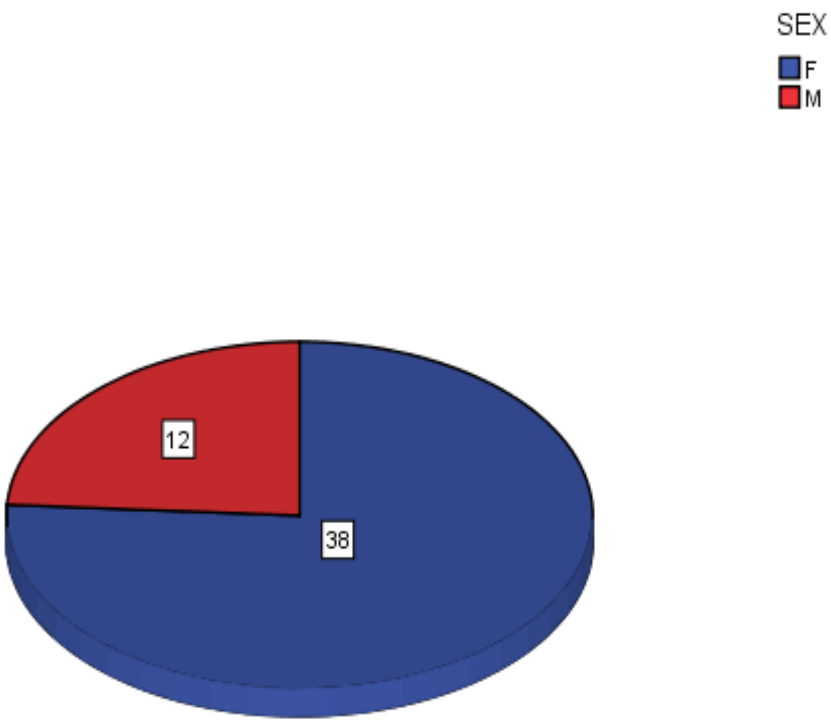


Table 4 **.BASELINE CLINICAL AND LABORATORY PROFILE**

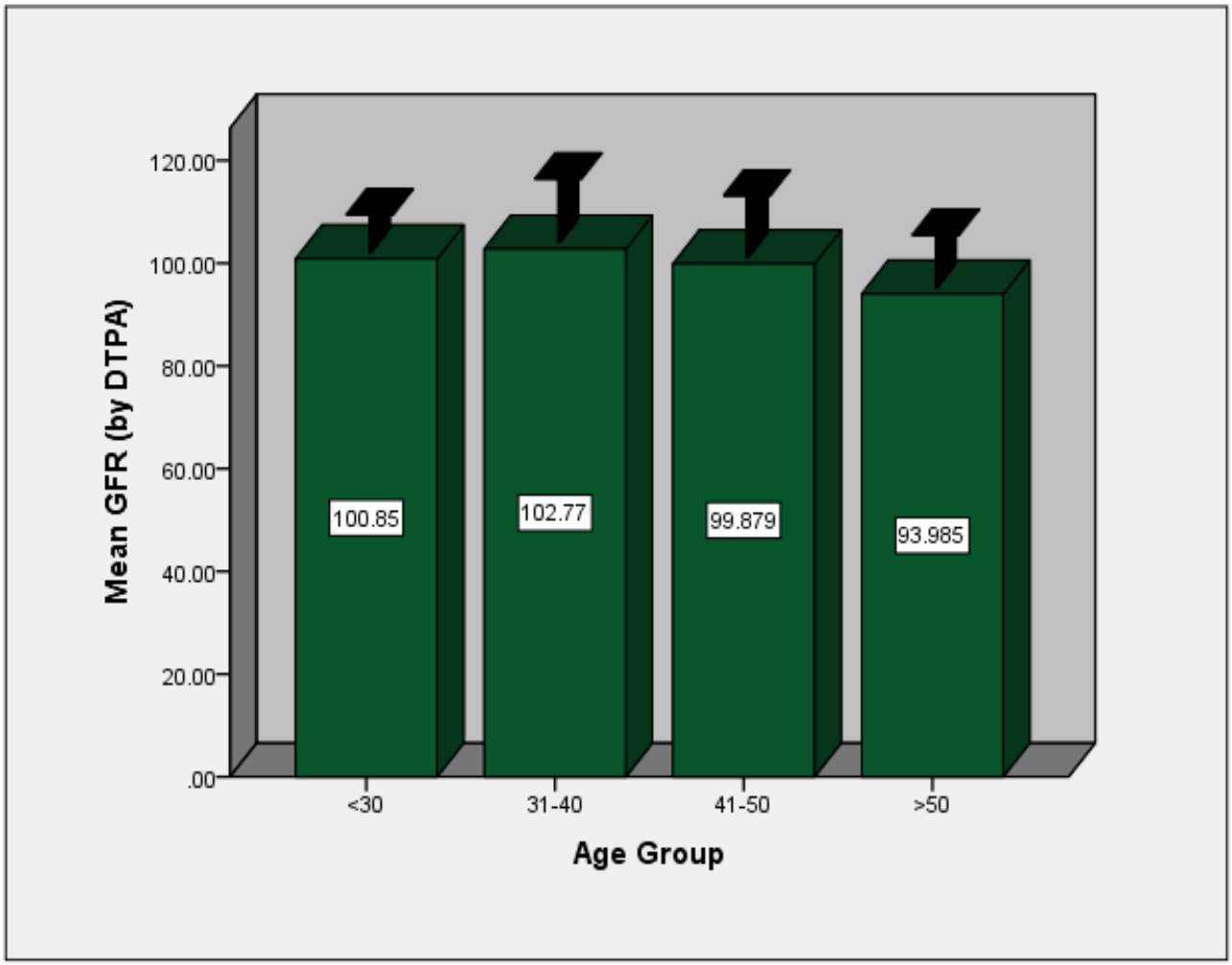
PARAMETES	**MEAN**	**MEDIAN**	**STD**	**SE OF MEAN**	**RANGE**
AGE	43.42	45	9.35	1.32	31
BODY. WT(kg)	58.66	59	5.24	0.74	22
24 hr UP	133.18	132.50	27.39	3.87	95
Hb gms%	10.8	10.85	1.18	0.17	4.6
RBS mg/dl	123.62	121.0	26.22	3.71	95
BUN	10.84	9.6	3.72	0.53	18.8
S.CREATININE	1.01	1.0	0.18	0.03	0.8
S.ALBUMIN	4.1	4.1	0.23	0.03	1.1

Table 5 :DISTRIBUTION OF GFR (DTPA) IN VARIOUS AGE GROUPS:

AGE GROUP(years)	SEX	GFR BY DTPA SCAN			
		MEAN	MEDIAN	SD	RANGE
>30	Male	107	107	-	-
	Female	99.8	101.5	7.9	21
31-40	Male	111.5	110	5.7	12
	Female	97.8	94	13.4	32.5
41-50	Male	105.7	105	13	26
	Female	98.8	99	12.5	41.8
>50	Male	98.6	100	14.2	31.6
	Female	91.9	92	9	27.6

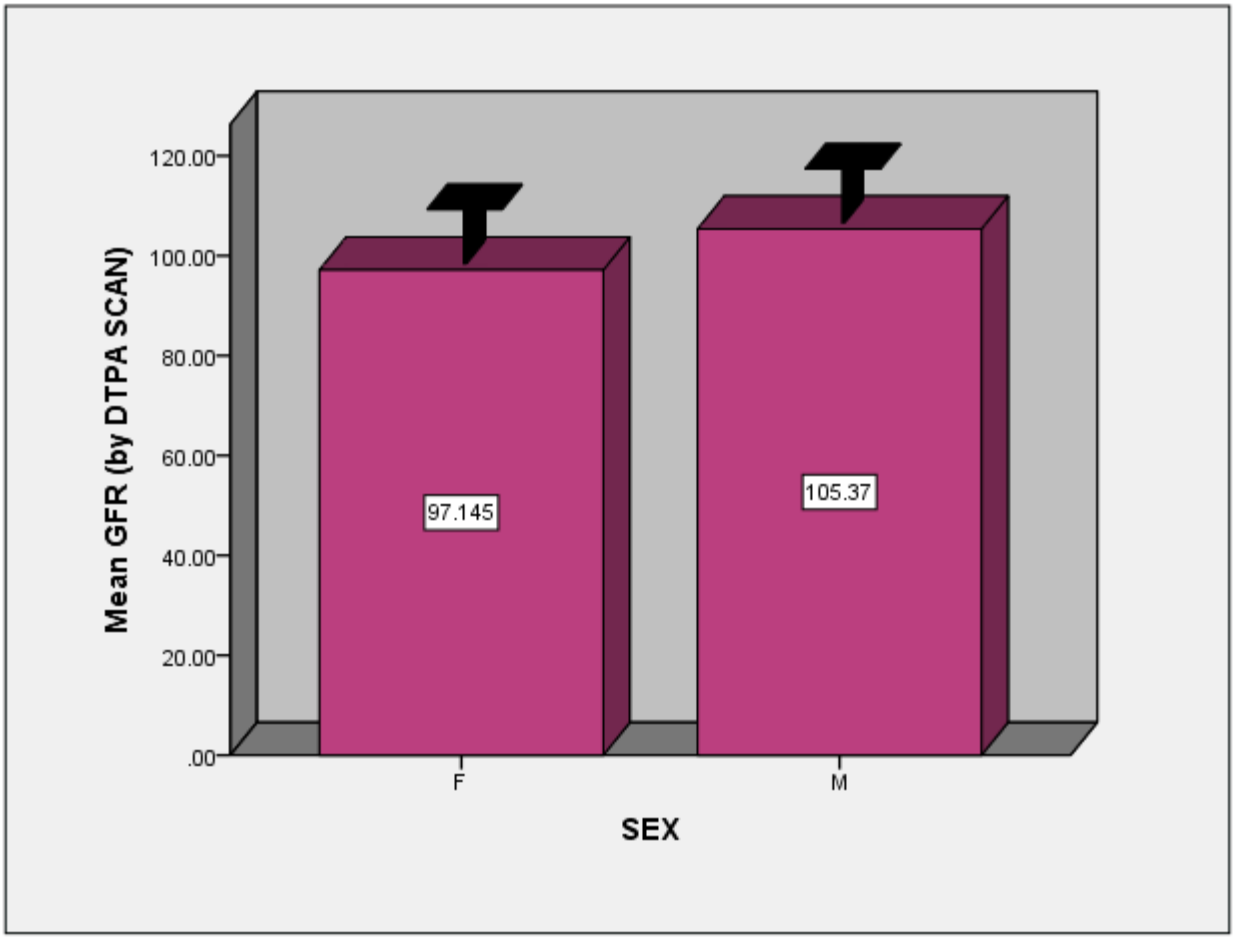
This table shows that the mean GFR calculated by DTPA scan of is higher in the males than the females and mean GFR is maximum in the age group of 31-40 years and mean GFR decreases as age advances

Chart 3 . MEAN GFR AND AGE GROUP ANALYSIS



Error bars: +/- 1 SD

Chart 4 . MEAN GFR AND SEX DISTRIBUTION ANALYSIS



Error bars: +/- 1 SD

GFR is calculated by downloadable calculators for the respective equations and their mean, median, standard deviation and standard error of mean are tabulated

Table 6 .GFR BY VARIOUS METHODS

METHOD	MEAN	MEDIAN	STD. DEVIATION	STD. ERROR OF MEAN
C-G	71.23	67.11	16.75	2.37
MDRD	71.82	69.63	16.75	2.37
CKD-EPI	76.50	73.50	17.84	2.5
DTPA SCAN	99.12	99.47	11.73	1.66

[C-G-cockcroft-gault]

Thus it is inferred from the above that the mean GFR calculated by DTPA > CKD-EPI > MDRD > C-G. The standard error of mean is 2.37, 2.37, 2.5, 1.66 for Cockcroft-Gault, MDRD, CKD-EPI equations and DTPA scan respectively.

Chart 5 : MEAN GFR BY VARIOUS METHODS

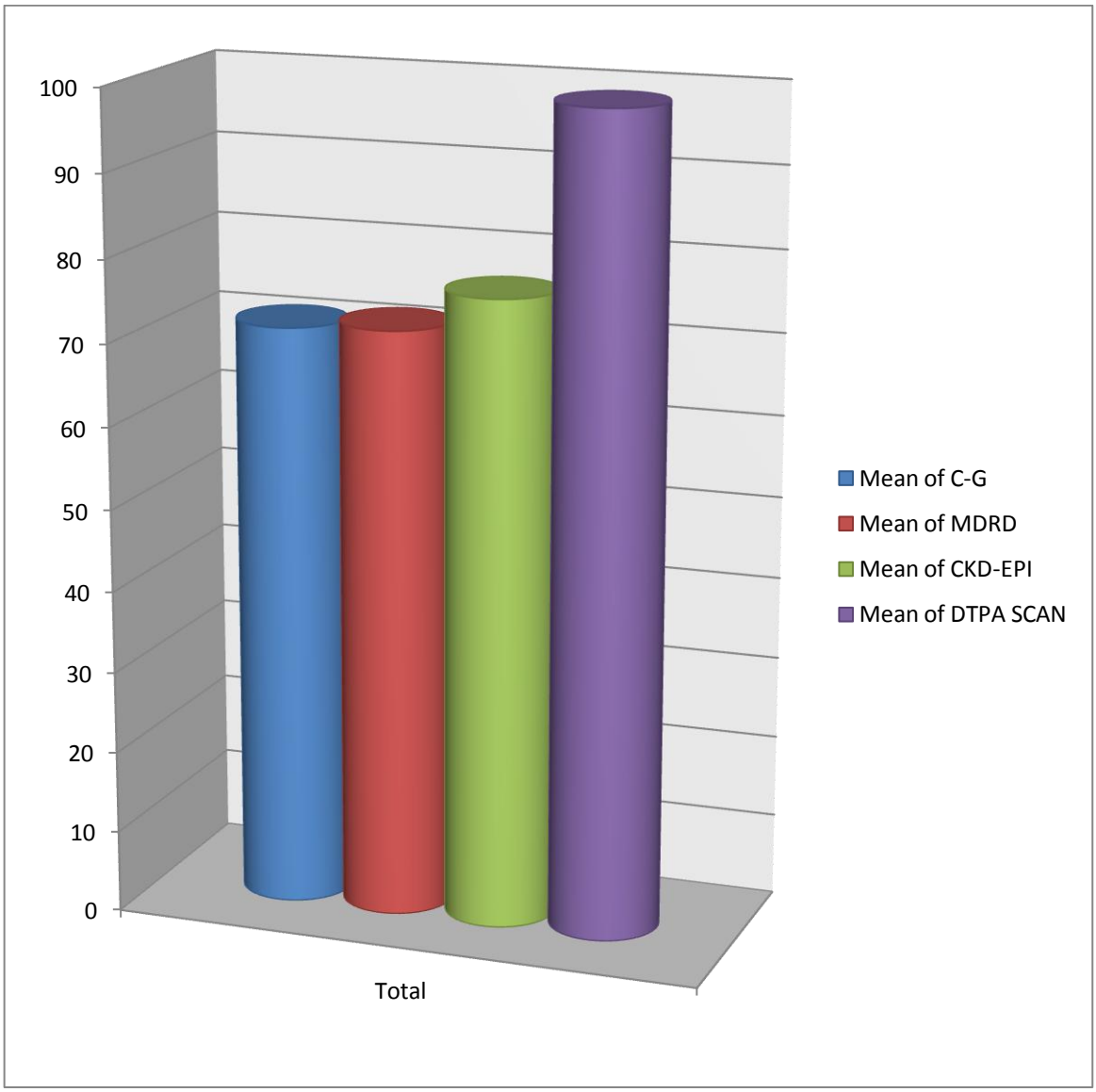


Table 7 .COMPARISON OF DIFFERENCE IN GFR FROM DTPA SCAN:

METHOD	MEAN GFR	MEAN DIF DTPA	MEDIAN DIF. DTPA	STD DIF. DTPA	MEAN% DIF. DTPA
C-G	71.23	27.88	28.95	17.93	27.65
MDRD	71.82	27.30	28.45	17.27	27.17
CKD-EPI	76.50	22.62	23.5	18.09	22.42

After calculating the mean GFR, their difference from the DTPA scan was calculated. The difference in GFR was much lesser in case of CKD-EPI formula when compared to MDRD and COCKCROFT-GAULT. The median difference from DTPA and the mean percentage difference were lesser with CKD-EPI formula.

Thus it is seen that the prediction equations, Cockcroft-gault, MDRD and CKD-EPI underestimated GFR by 27.65%, 27.17% and 22.42% when compared to DTPA renal scan

Table 8 . ACCURACY OF COCKCROFT-GAULT FORMULA:

% OF ERROR	NO. OF PATIENTS	% OF THE STUDY GROUP
<25	20	40
25-40	17	34
>40	13	26

Thus COCKCROFT-GAULT formula predicts GFR with < 25% error in almost 40% of patients,25-40% error in 34% of patients and >40% error in 26% of patients.

Table 9 .ACCURACY OF THE MDRD FORMULA:

% OF ERROR	NO OF PATIENTS	% OF THE STUDY GROUP
<25%	22	44
25-40%	18	36
>40%	10	20

Thus MDRD formula predicts GFR with <25% error in 44% of patients, 25-40% error in 36% of patients and >40 % error in 20% of patients.

Table 10 :ACCURACY OF CKD-EPI FORMULA:

% OF ERROR	NO OF PATIENTS	% OF THE STUDY GROUP
<25	25	50
25-40	18	36
>40	7	14

Thus CKD-EPI formula predicts GFR with <25% error in 50% of patients, 25-40% error in 36% of patients and >40% error in 14% of patients.

Chart 6 : ACCURACY OF COCKCROFT –GAULT FORMULA

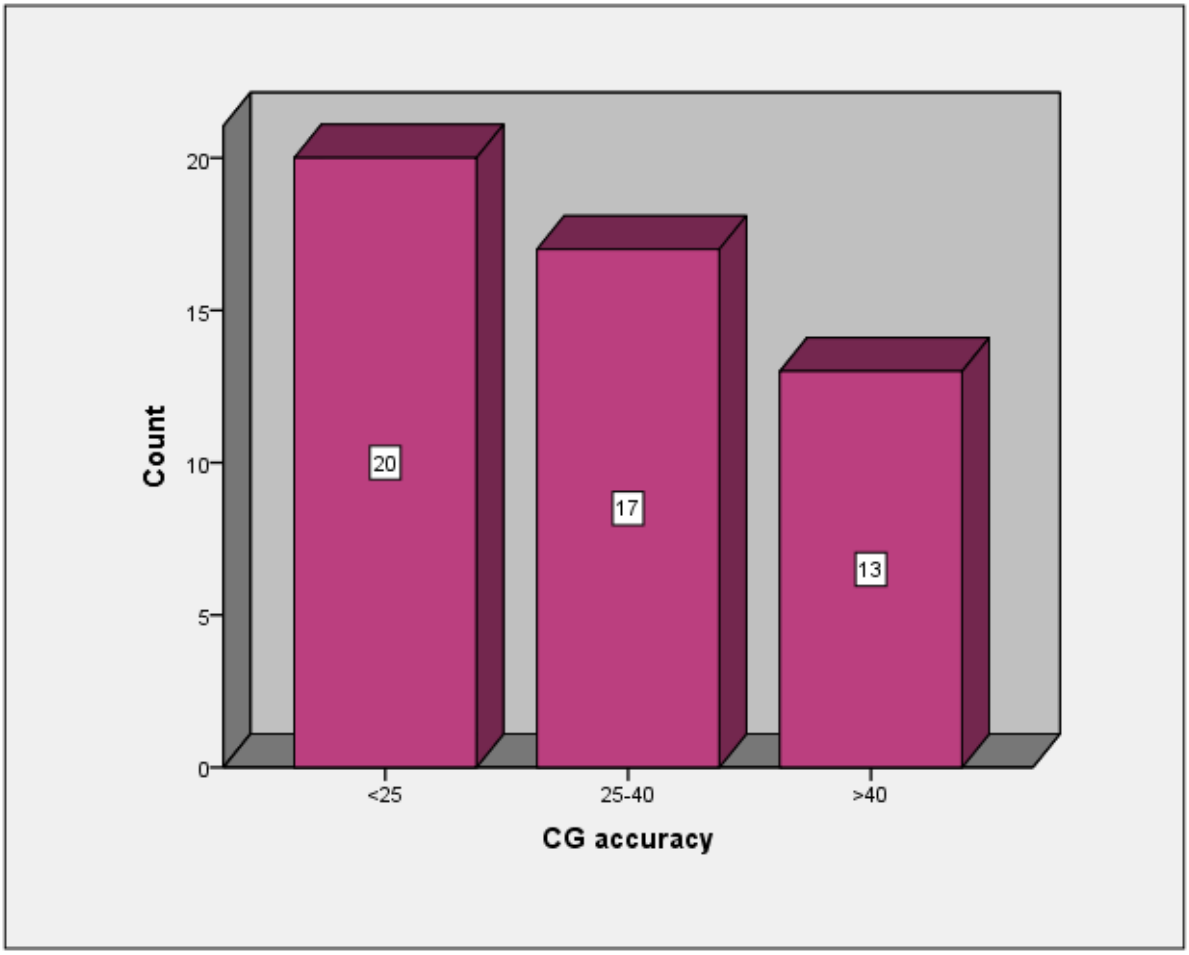


Chart 7 : ACCURACY OF MDRD FORMULA

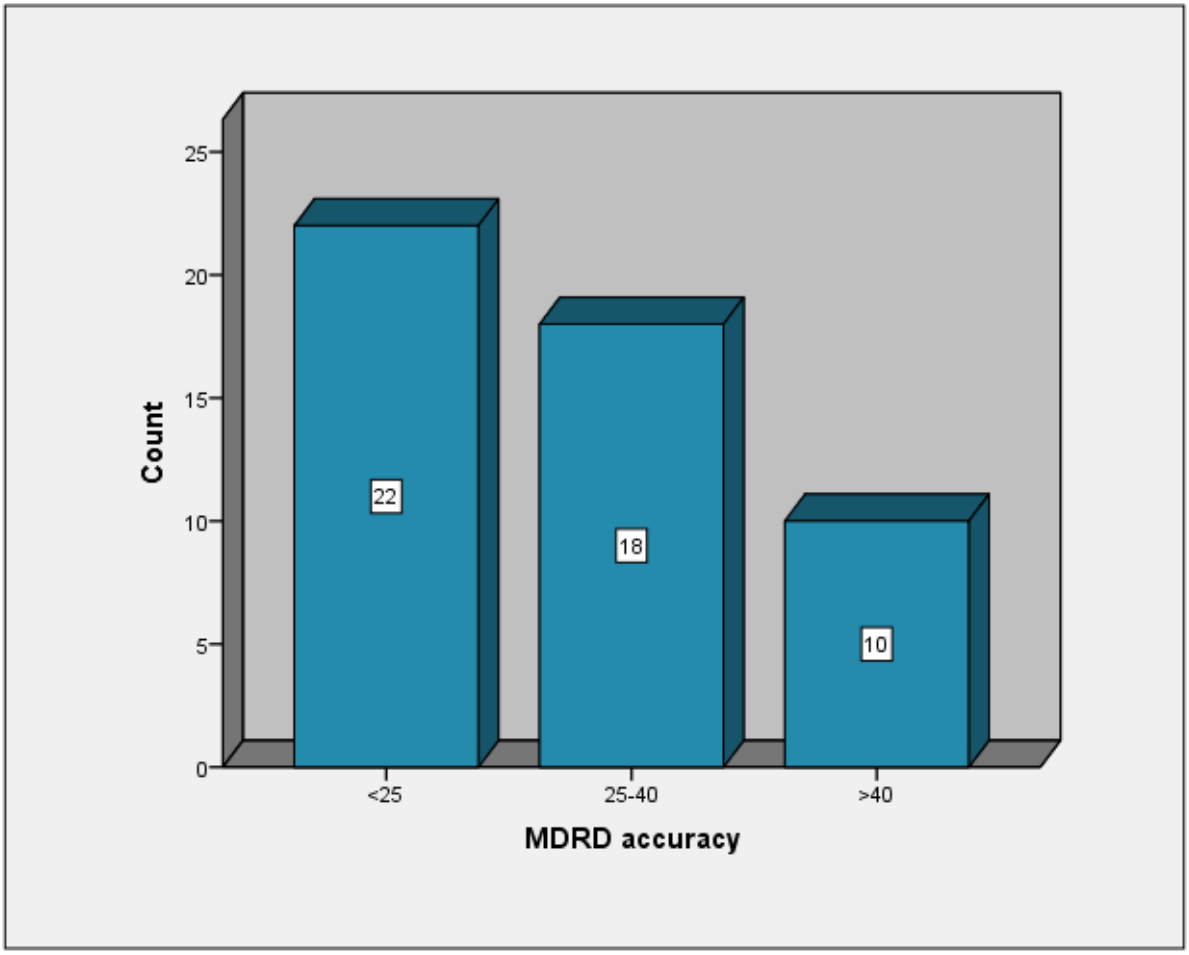


Chart 8 : ACCURACY OF CKD – EPI FORMULA

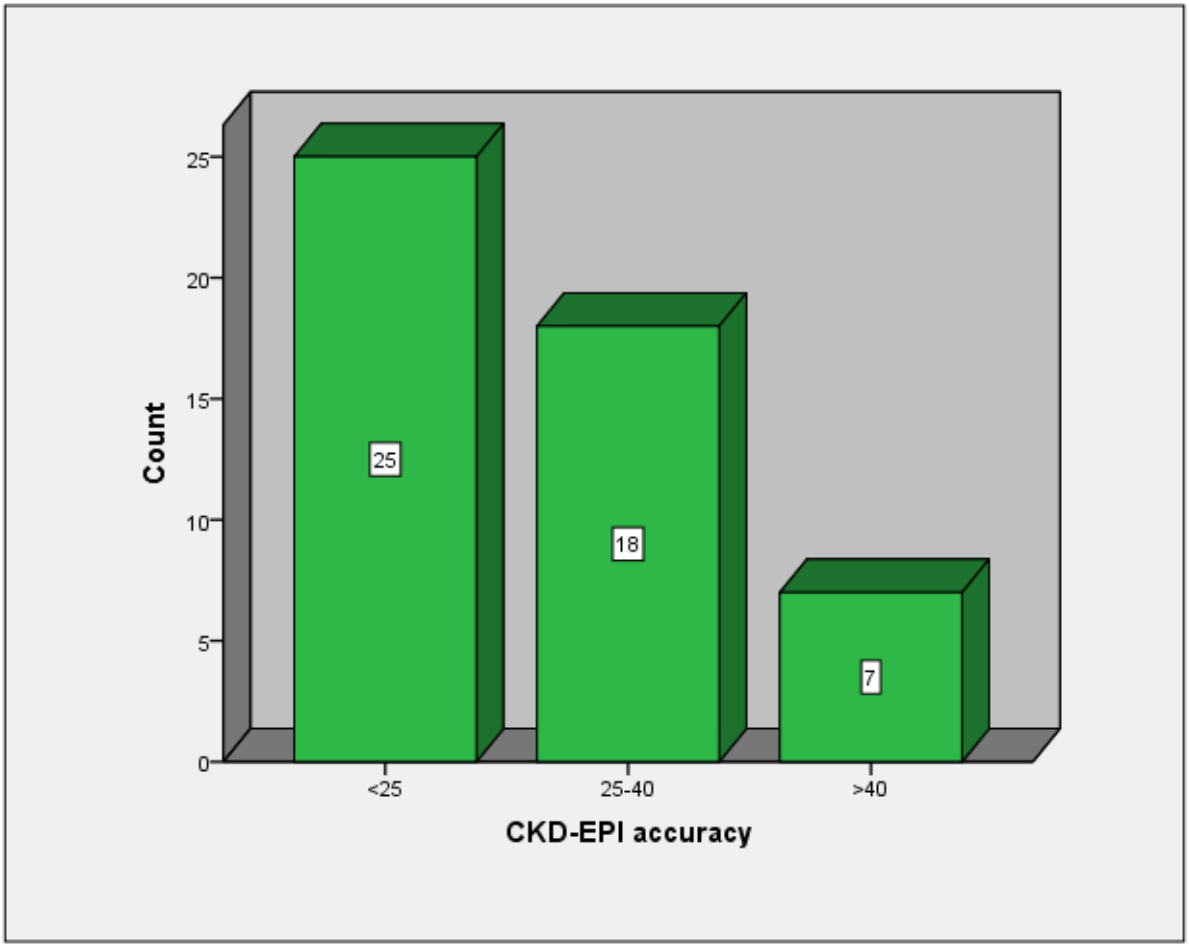


Table 12 : CORRELATION OF COCKCROFT-GAULT WITH DTPA SCAN

Pearsons coefficient ‘r’	0.246
Linear regression R^2	0.061
Significance2-tailed, [pvalue]	0.085

P –value of <0.05 was considered statistically significant , it is evident that there is a correlation between Cockcroft-Gault equation and DTPA but that is not a statistically significant correlation

Chart 9 : LINEAR REGRESSION PLOT OF DTPA AND CG

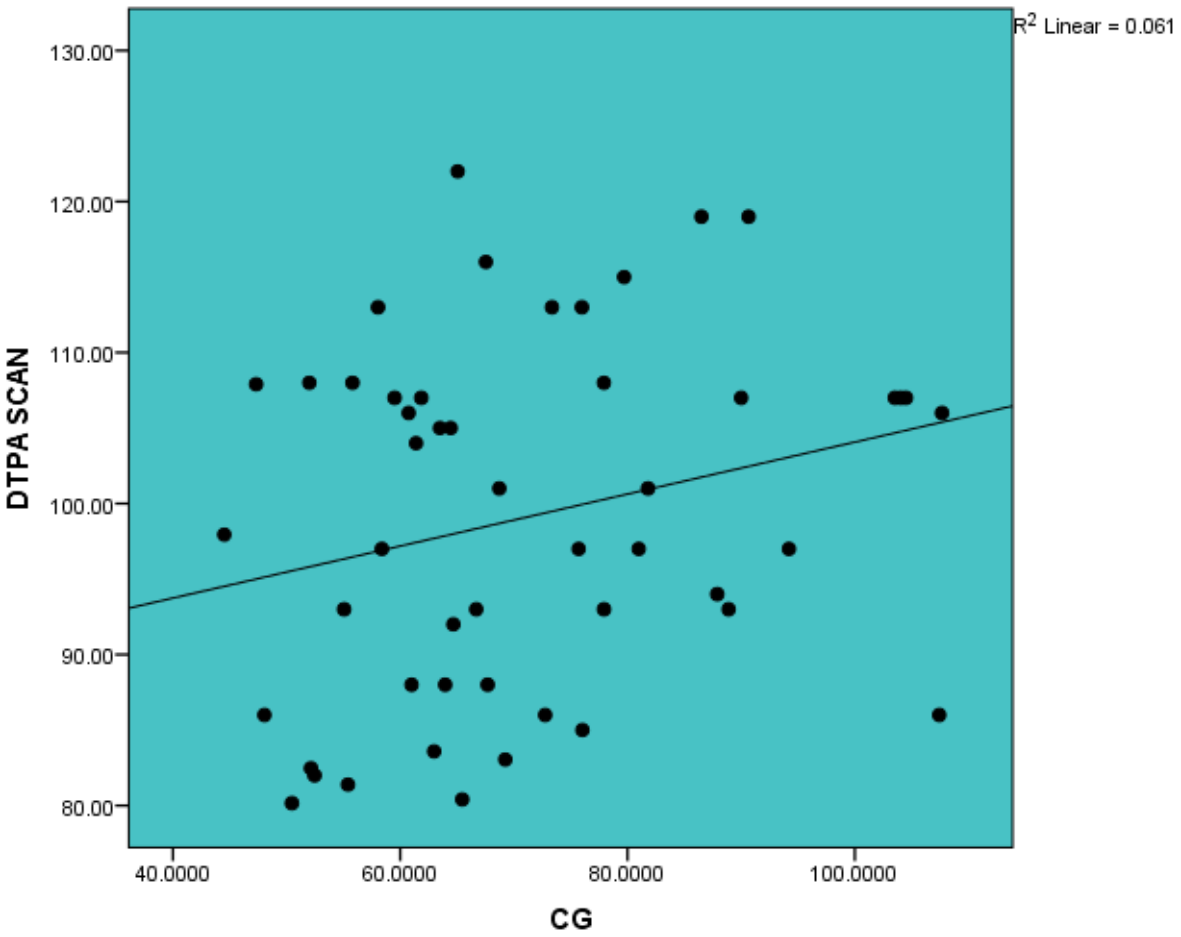


Table 13 : CORRELATION OF MDRD WITH DTPA SCAN:

Pearsons Coefficient, 'r'	0.305
Linear regression R^2	0.093
Significance -2 tailed [P value]	0.031

P- value of <0.05 was considered statistically significant and it is evident that there is a statistically significant correlation between MDRD equation and DTPA scan.

Chart 10 : LINEAR REGRESSION PLOT OF MDRD AND DTPA

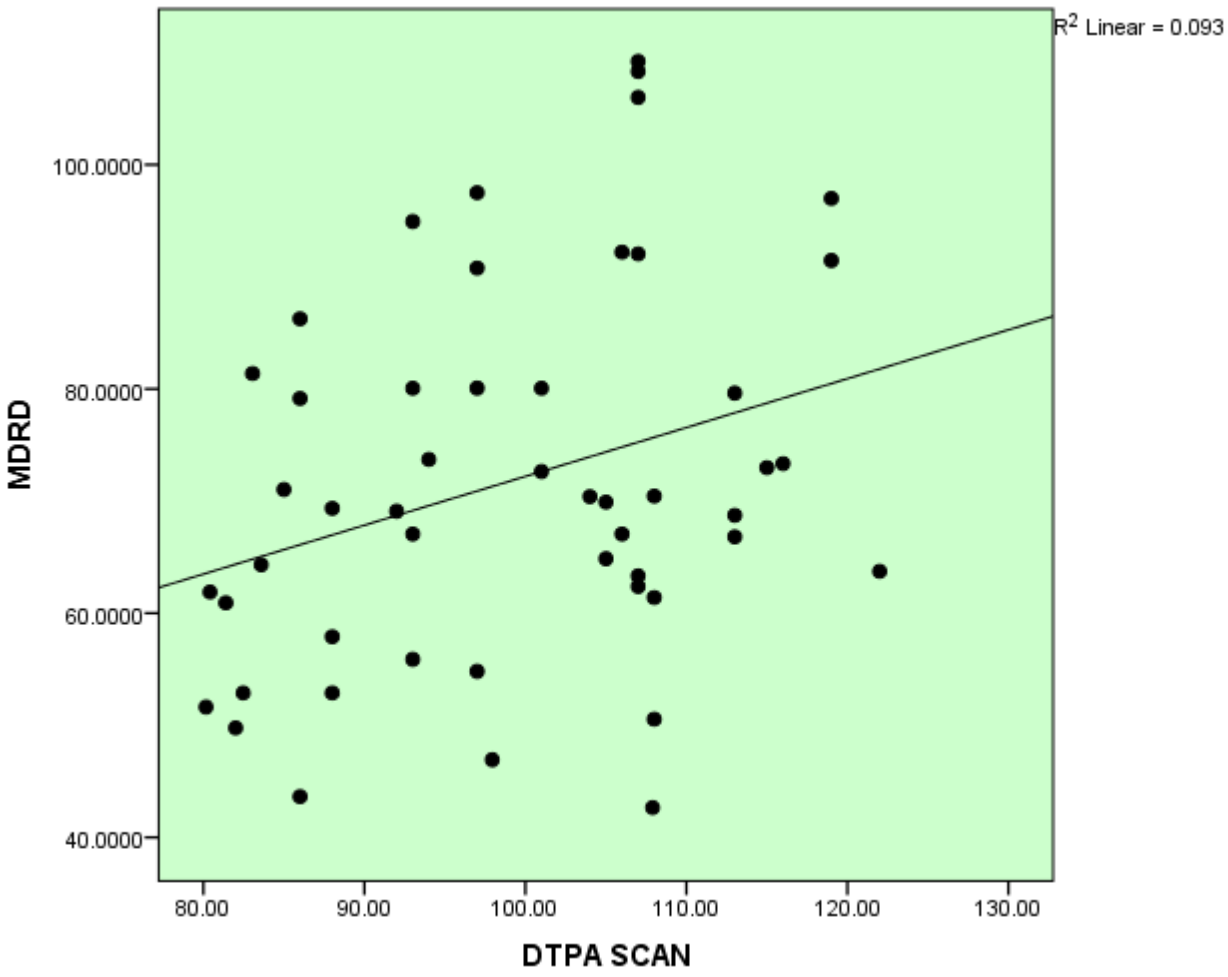


Table 14 :CORRELATION OF CKD-EPI WITH DTPA:

Pearsons coefficient, ‘r’	0.307
Linear regression R^2	0.094
Significance 2-tailed [P value]	0.03

P-value of <0.05 was considered as statistically significant, again there is a statistically significant correlation between CKD-EPI equation and DTPA scan

Chart 11 : LINEAR REGRESSION PLOT OF CKD-EPI AND DTPA

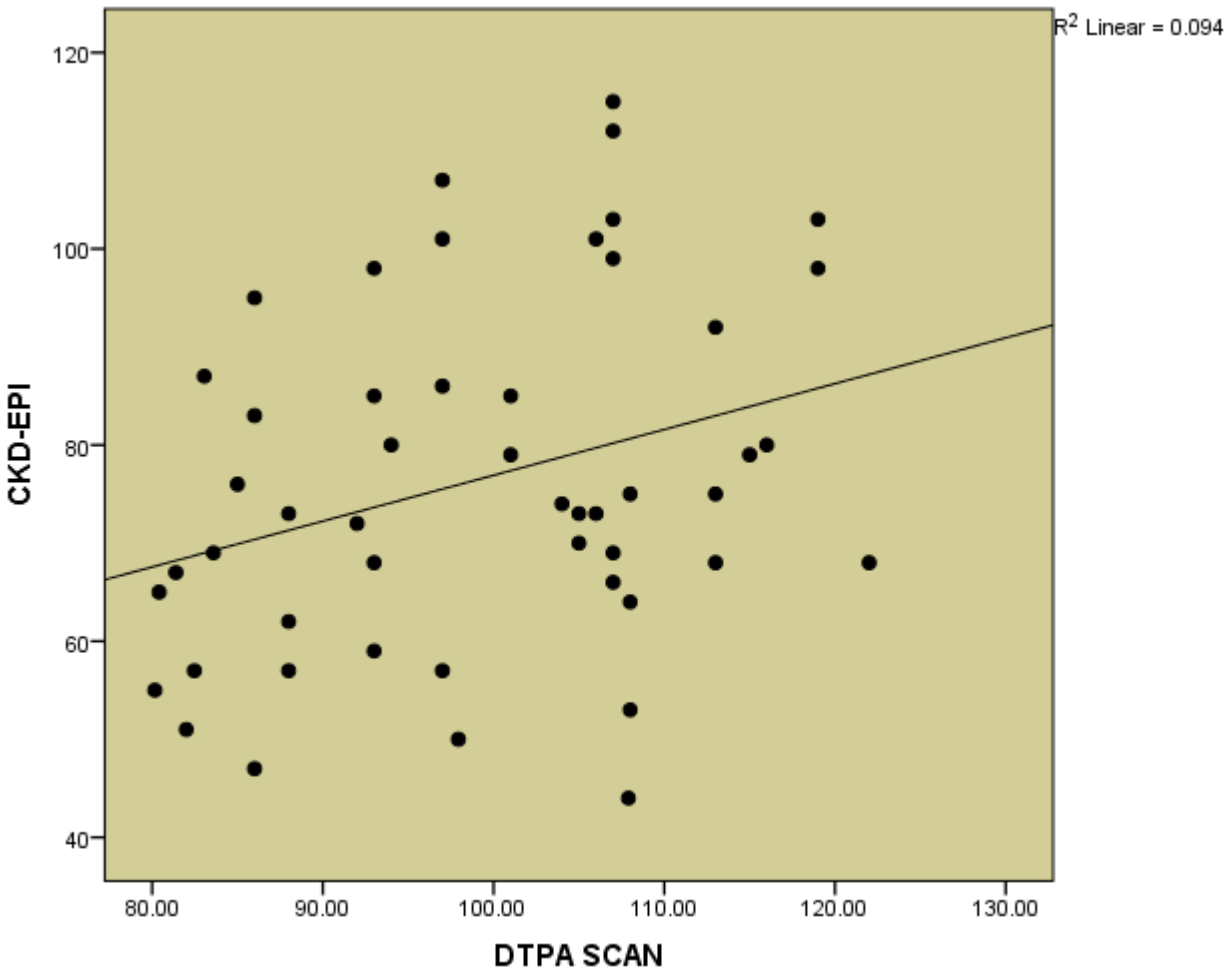


Table 15 : COMPARISON OF CO-EFFICIENT OF CORRELATION

FORMULA	COEFFICIENT OF CORRELATION	P-VALUE	SIGNIFICANCE
Cockcroft-Gault	0.246	0.085	Not significant
MDRD	0.305	0.031	Significant
CKD-EPI	0.307	0.030	Significant

Our study aims to compare three different methods (Cockcroft-Gault,MDRD, and CKD-EPI equations) with the gold standard method (DTPA scan), hence we apply Bland and Altman method to establish the concordance between them.

Chart 12 :BLAND & ALTMAN PLOT FOR C-G AND DTPA SCAN

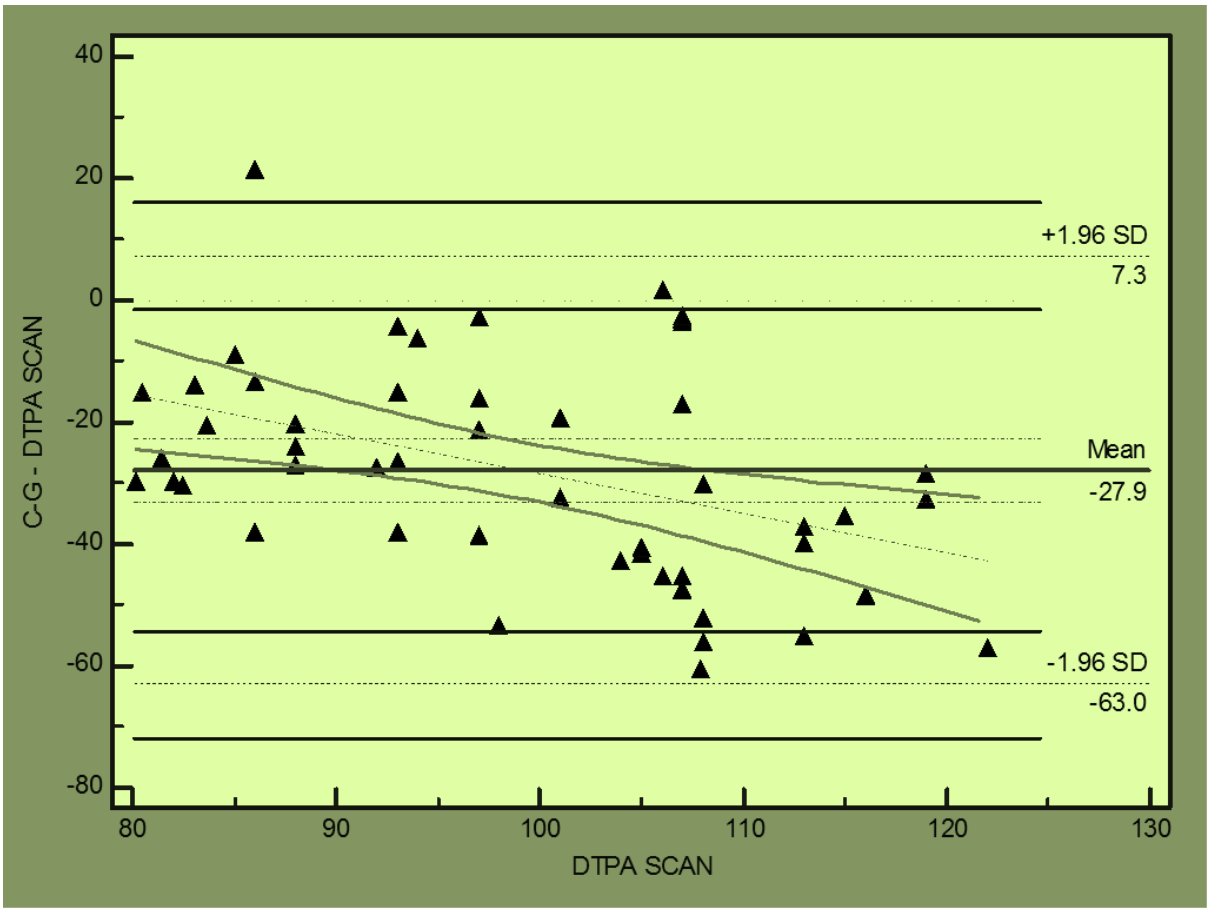


Chart 13 : BLAND & ALTMAN PLOT FOR MDRD AND DTPA SCAN

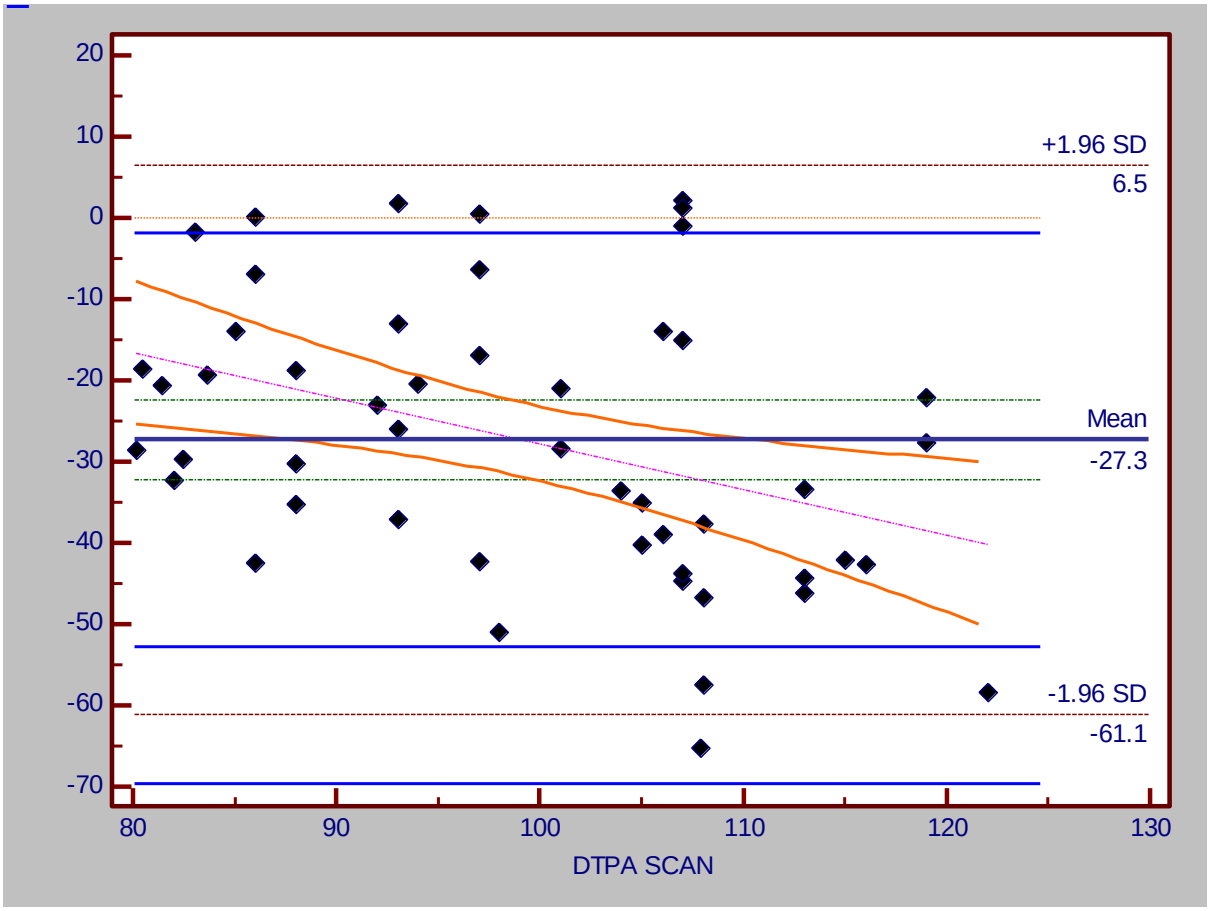


Chart 14 : BLAND & ALTMAN PLOT FOR CKD – EPI AND DTPA SCAN

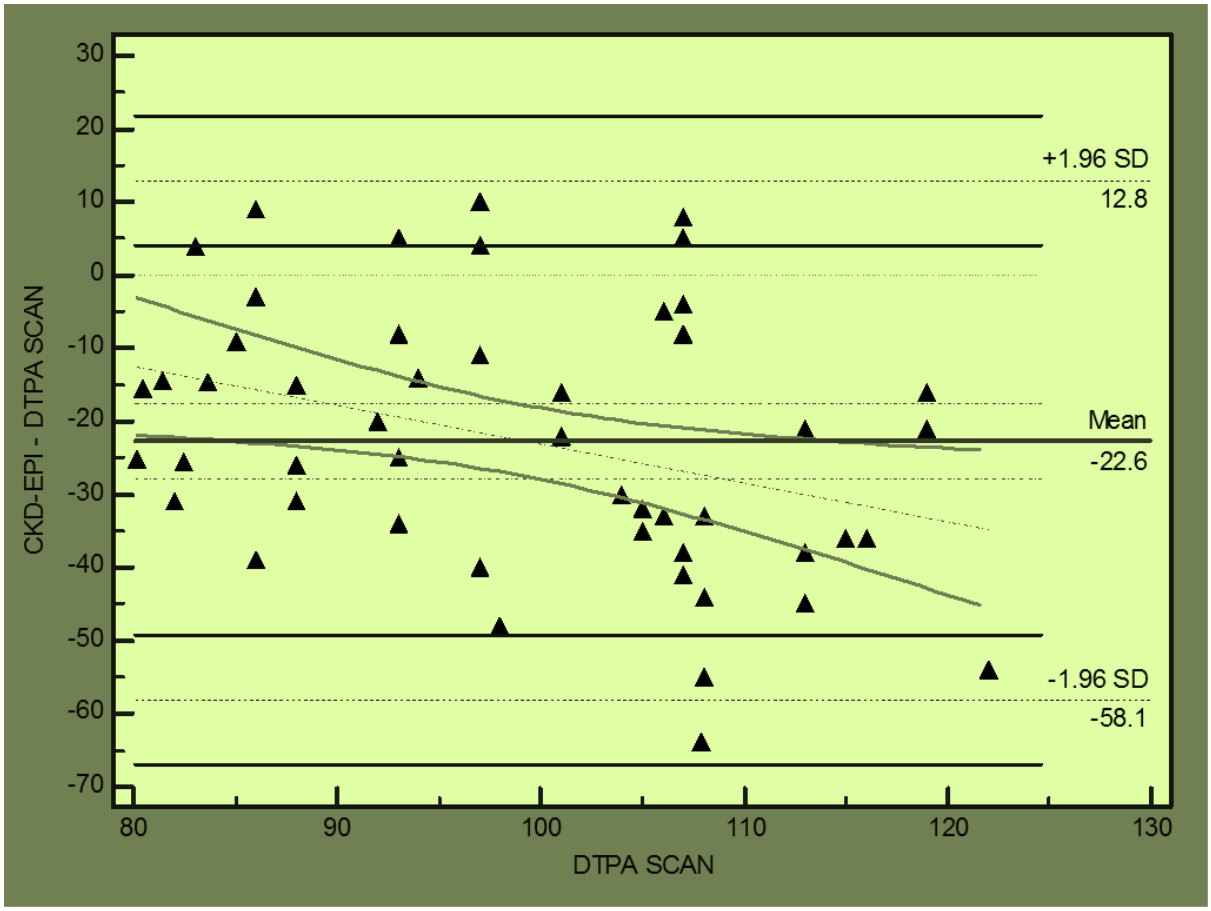


TABLE 15 : CONCORDANCE ANALYSIS OF C-G , MDRD,& CKD-EPI

COMPARISON WITH DTPA	CONCORDANCE INTERVAL		CONFIDENCE INTER VAL	MEAN DIFFERENCE IN GFR
	UPPER LIMIT	LOWER LIMIT		
COCKCROFT GAULT	7.3	-63	95%	27.9
MDRD	6.5	-61.1	95%	27.3
CKD-EPI	12.8	-58.1	95%	22.6

It is obvious that majority of the plots are clustered around the mean line with a confidence interval of 95%, however these equations tend to underestimate GFR at all the levels with a mean difference of 27.9ml/min, 27.3ml/min and 22.6ml/min for Cockcroft-Gault, MDRD, and CKD-EPI respectivel

DISCUSSION

Chronic kidney disease is a global (CKD) problem, gaining importance day by day. CKD burden increases due to

-increased prevalence of hypertension, diabetes and cardiovascular diseases

-better availability of the treatment

-decrease in mortality and morbidity

There are studies, which show that the prevalence of early CKD is much greater than the prevalence of late CKD [27]. Hence early detection of CKD and initiation of treatment measures to halt its progression is the need of the hour.

The concept of using serum creatinine as a marker of GFR is not validated in most of the clinical settings .Since a 50 % fall in GFR is necessary for the creatinine level to rise, it is high likely that early cases of CKD may be missed. GFR can be estimated using prediction equations, again these equations employing serum creatinine depends on the calibration and variability of the method used[28].However the new K/DOQI guidelines recommend use of prediction equations in estimating GFR [2].

Our study, an observational study involving 50 prospective renal donors employed various prediction equations (Cockcroft-gault, MDRD, CKD-EPI) to estimate GFR and compared their values with DTPA renal scan.

The mean GFR estimated by Cockcroft-gault, MDRD and CKD-EPI formula were 71.23, 71.82 and 76.50; likewise the mean difference from DTPA scan were 27.86, 27.30 and 22.62 respectively. Thus it is obvious the prediction equations significantly underestimates the GFR. However there was a fair amount of correlation of these prediction equations with the DTPA scan values, where CKD-EPI correlating better among the three

.Cockcroft-Gault formula does not correct for race of the individuals, also our study group comprised of predominantly of elderly females. The serum creatinine not being calibrated with standard measurements, could be another reason for underperformance of the Cockcroft-Gault .

MDRD formula was devised , based on the creatinine clearance of the CKD population. Our study group being normal individuals, might contribute for underperformance of the MDRD. There were studies where MDRD underestimated GFR upto 29% [29]. Again errors in caliberating

serum creatinine might be a potential reason for underperformance of the MDRD[30].

Regarding the CKD-EPI formula , it was introduced recently and was not validated in different clinical studies. Although limited references states that CKD-EPI performs better than MDRD [16],[23]. In our study CKD-EPI also underestimates GFR, with a mean of 76.50 ml/min where mean GFR measured by DTPA was 99.12 ml/min. The possible causes could be the predominant study population being elderly females, none of them being African-American, and errors in serum creatinine estimation. It requires creatinine estimation by isotope dilution mass spectrometry, which again could be a setback in our study.

There were many studies reported in the literature , comparing the predicting equations namely Cockcroft-Gault and MDRD. In the Levey et al study [31] ,1628 CKD patients where included and the mean GFR was 48.6. The creatinine clearance estimated by 24 hour urine creatinine clearance and the Cockcroft-Gault overestimated GFR BY 16% but MDRD performed better in them.In the Lewis et al [32] study 1703 African –American patients with CKD were included, where the mean GFR was 56.8. Here Cockcroft-Gault underestimated GFR and MDRD estimated GFR accurately, the study population being the CKD patients MDRD performed better in these studies .In Bertolus et al study [33], 22 potential

donors with creatinine clearance <80ml/min were included, and showed both the equations performed poorly and it suggested to index serum creatinine by height rather than body surface area .

In the Bostom et al study [34], 109 CKD patients were included , showed MDRD was a much precise equation , but considering the multiple possibilities of error the equation has to be used with caution. Measurement of GFR using markers like Inulin, DTPA, Iohexol and Iothalamate being cumbersome MDRD may be used to estimate GFR in patients with early CKD.

In the Vervootet al [35] study, 46 healthy adults and 46 type 1 diabetics without proteinuria were included and showed that the MDRD equation performed poorly in the diabetics. In the Kingdon et al [36] study, 26 patients with scleroderma were included and they found that the MDRD equation employing demographic and serum variables performed excellently in those patients .In the Poggio et al study [40], MDRD equation overestimated GFR in CKD patients and both MDRD and Cockcroft-Gault equations underestimated GFR in patients with normal kidney function. In the Rule et al study[42], as a result of sub optimal accuracy of the prediction equations they cannot be generalized and new prediction equations based on markers like cystatin-C needs to be devised. They are not reliable in potential kidney donors.

Studies	Sample Size	Study population	Mean Age	Mean Wt	Mean GFR	R^2 CG	R^2 MDRD
Levey et al 1999 [31]	1628	CKD patients	51	79.6+/- 16.8	48.6	NR	0.9
Lewis et al 2001 [32]	1703	Blacks with CKD	54	90.2	56.9	0.85	0.9
Bertolus et al 2001 [33]	22	Donors with crcl <80ml/min	40	71.5	99.3	0.14	0.005
Bostom et al 2002 [34]	109	CKD cohort	43	76	109	0.17	0.31
Vervoot et al 2002[35]	92	46 healthy adults 46 T1DM	28/27	69.9/ 70.5	107/ 122	NR	NR
Kingdon et al 2003 [36]	26	Scleroderma pts	58	NR	NR	NR	0.79
Our study	50	Normal /potential Donors	43.42	58.66	99.12	0.061	0.093

Although all these studies have employed Cockcroft-gault and MDRD equations none employed CKD-EPI. Only few studies were reported , which employs CKD-EPI equation. A research article from France[37] , states that prediction equations (MDRD, CKD-EPI) created discrepancy in epidemiological assessment of CKD prevalence.

A study in Australia in 2010 [38] showed , the prevalence of CKD in the Australian population aged more than 25 years, using MDRD was 13.4% , the prevalence was 11.5% using CKD-EPI , this was because 266 individuals in the study who belonged to the CKD group, according to MDRD equation were reclassified as not having CKD by the CKD-EPI , due to better estimation of GFR .

Another study in Netherlands [39] , stated that both MDRD and CKD-EPI were able to predict with higher accuracy when compared to other equations .Lin et al study[41], the MDRD equation underestimates GFR, and the Cockcroft-Gault equation consistently overestimates measured GFR in people with normal kidney function. In potential kidney donors, prediction equations may not be sufficient for estimating GFR and radioisotope studies like DTPA SCAN may be needed for a better assessment of GFR.

In a Chinese study of comparing the prediction equations in potential live kidney donors [43] all the prediction equations performed poorly and considering the importance of the kidney transplantation more accurate methods of GFR calculation needs to be devised .

Another study from Thailand [44] included 60 healthy adults, and found that the prediction equations were suboptimal, and suggested newer methods for employing prediction equations among various ethnic groups.

Winding up, in our study on 50 potential donors, the prediction equations namely Cockcroft-gault, MDRD and CKD-EPI underestimated GFR by 27.65%, 27.17% and 22.42% respectively when compared to DTPA renal scan.These equations were able to predict GFR with <25% error in 40%, 44% and 50% of the study group for Cockcroft-Gault , MDRD, and CKD-EPI respectively.

However all these 3 equations were found to correlate with DTPA scan values, the correlation was statistically significant for MDRD and CKD-EPI, and statistically not significant for Cockcroft-Gault equation

.Hence it is inferred that these prediction equations cannot be solely relied upon in case of clinical settings like renal transplantation and so further research is required for devising newer methods which could be

applicable in all the clinical settings, all age groups, both sexes, and all ethnic groups !!

LIMITATIONS OF THE STUDY:

- very small sample size
- African Americans were not included in the study
- study group predominantly comprises of females
- the values were not calibrated with standard measurements
- the source of error could possibly be intra-individual variability in serum creatinine, laboratory methods, GFR per se and GFR measurement

SUMMARY AND CONCLUSIONS:

- The prediction equations namely Cockcroft-Gault, MDRD and CKD-EPI were found to correlate with the DTPA scan values.
- However they underestimated GFR by 27.65%, 27.17% and 22.42% respectively, the possible reasons could be

-lack of standardization in calibration of serum creatinine

-study population predominantly being females

-sample size was small

-African –Americans were not included in the study

-MDRD and Cockcroft-Gault were devised in the CKD setting and not in the normal population , our study group belonged to normal and healthy adults.

- These prediction equations were not validated in our population and our clinical set up.
- DTPA scan gives split GFR of each kidney, renal tubular function, details about renal blood supply, renal tubular obstruction or damage
- DTPA scan cannot be substituted by the prediction equations in special situations like renal transplantation

- However extensive research work are under process , which may bring out newer, more accurate, less invasive and cheaper ways of estimating GFR which can be applicable in all the clinical settings.
- Let us hope we achieve that in the near future.

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INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work	: A comparative study of glomerular filtraction rate calculation by COCKROFT-GAULT formula, MDRD formula,CKD-EPI formula and DTPA renal scan among live related kidney donors –
Principal Investigator	: Dr.K.Senthamizh Selvan PG in MD(GM)
Designation	: PG in MD(GM)
Department	: Department of Medicine Government Stanley Medical College, Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 18.04.2011 at the Modernized Seminar Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate form the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI

PROFORMA

Serial number :

Date :

Name :

Age :

Sex :

Address :

Contact phone number :

Occupation :

Relation to the patient :

Body weight in kg :

History of diabetes /hypertension :

Family history of renal disease :

Pulse : Blood pressure :

Cardiovascular system :

Respiratory system :

Urine : albumin, sugar, deposits

24 hour urine protein :

Hemoglobin :

Bleeding time :

Clotting time :

Random blood sugar :

Blood urea nitrogen (mg/dl) :

Serum creatinine (mg/dl) :

Serum albumin (g/dl) :

Ultrasonogram abdomen :

DTPA renal scan report :

S.N.	NAME	AGE	SEX	RELATION	WT.KG	HT/DM	F. H/O.R. D	BP	24 Hr UP	Bl.G	Hb	BT	CT	RBS	BUN	S.Cr	ALB	USG	C-G	MDRD	CKD-EPI	DTPA
1	sakunthala	52	F	mother	60	no	no	130/80	180	B	10.5	2	5	140	8.4	0.8	3.9	N	77.93	80.06	85	93
2	gandhimathi	50	F	mother	57	no	no	124/76	140	O	9.3	1	4	135	7.9	0.8	4	N	75.7	80.07	86	97
3	jeyanthi	41	F	sister	52	no	no	110/70	110	A	11	2	4	124	7.9	0.9	4.5	N	67.53	73.34	80	116
4	Jothi	26	F	sister	64	no	no	120/76	160	B	11.8	1	6	150	7.4	0.8	4.2	N	107.67	92.2	101	106
5	sardhani	35	F	sister	49	no	no	110/70	120	O	9.8	2	6	160	14.4	1	4.4	N	60.74	67.06	73	106
6	kalaiselvi	50	F	mother	66	no	no	138/80	135	B	10.9	2	4	110	7.9	0.9	3.9	N	77.92	70.44	75	108
7	ramakrishnan	33	M	brother	63	no	no	120/84	115	AB	12	1	3	130	9.4	0.9	4.1	N	104.03	109.21	112	107
8	kuppammal	42	F	mother	57	no	no	116/76	100	B	10	2	5	108	7.4	0.7	3.9	N	94.2	97.5	107	97
9	muniammal	48	F	mother	61	no	no	130/80	137	O	8.9	1	4	97	19.8	1.4	4.1	N	47.32	42.66	44	107.9
10	kanniammal	28	F	daughter	49	no	no	108/76	123	B	9.7	3	6	117	8.9	0.8	4.3	N	80.99	90.78	101	97
11	shantha	50	F	mother	59	no	no	130/80	165	B	11.4	2	3	141	14.9	1.2	4	N	52.24	50.54	53	108
12	Malar	40	F	mother	67	no	no	124/80	115	A	10.9	1	4	109	8.9	0.9	4.8	N	87.89	73.71	80	94
13	Mallika	55	F	mother	58	no	no	136/84	140	B	9	2	6	145	8.4	0.9	4.4	N	64.67	69.09	72	92
14	anushya devi	48	F	sister	~~51~~	no	no	126/80	155	A	11	1	5	118	7.9	0.8	4.1	N	69.24	81.37	87	83.05
15	sulthan basha	32	M	brother	60	no	no	130/76	110	B	13	2	4	157	13.9	1	4.5	N	90	92.04	99	107
16	Pattu	54	F	mother	55	no	no	140/80	165	O	10.7	3	5	132	11.9	1	4	N	55.8	61.4	64	108
17	bhuvaneshvari	29	F	sister	55	no	no	110/72	95	O	9.8	1	4	155	19.3	1.5	4.1	N	48.05	43.64	47	86
18	Ponni	30	F	sister	48	no	no	126/80	140	AB	11	2	5	110	20.8	1.4	4.2	N	44.52	46.93	50	97.94
19	Baby	36	F	sister	70	no	no	130/80	165	B	9.8	3	6	98	8.4	0.8	3.9	N	107.43	86.26	95	86
20	dhanalakshmi	54	F	mother	62	no	no	110/80	170	B	8.9	2	7	160	13.9	1.2	4.1	N	52.46	49.76	51	82
21	Uma	43	F	mother	55	no	no	126/70	110	O	10.7	1	2	90	13.9	1	3.9	N	62.98	64.32	69	83.59
22	annammal	50	F	mother	52	no	no	110/80	135	AB	9.9	3	5	115	15.8	0.9	4	N	61.39	70.4	74	104
23	Kaveri	42	F	sister	58	no	no	122/80	108	A	10.9	2	6	88	13.9	1.1	4.2	N	61	57.9	62	88
24	rajathee	50	F	mother	56	no	no	136/82	98	B	9	1	4	92	9.9	1	4.2	N	59.5	62.38	66	107
25	vasantha	54	F	mother	60	no	no	110/70	155	O	11.2	3	6	141	8.9	0.9	4.1	N	67.69	69.35	73	88

S.N.	NAME	AGE	SEX	RELATION	WT.KG	HT/DM	F. H/O.R. D	BP	24 Hr UP	Bl.G	Hb	BT	CT	RBS	BUN	S.Cr	ALB	USG	C-G	MDRD	CKD-EPI	DTPA
26	dhanalakshmi	48	F	mother	63	no	no	136/80	130	B	10.1	1	3	109	8.9	0.9	4.4	N	76.03	71.03	76	85
27	Vijaya	45	F	mother	54	no	no	110/72	105	O	11.3	2	7	143	13.9	1.2	4.6	N	50.47	51.63	55	80.16
28	bhavani	55	F	mother	58	no	no	108/76	160	A	10.7	1	3	97	7.4	0.8	3.9	N	72.75	79.15	83	86
29	chinnakulanthai	40	F	sister	65	no	no	130/76	95	B	9.3	3	4	130	13.9	1.2	4.5	N	63.95	52.88	57	88
30	Emili	52	F	mother	63	no	no	120/80	130	AB	11.2	2	6	108	8.9	0.8	4	N	81.8	80.06	85	101
31	Sathya	24	F	daughter	51	no	no	108/70	95	B	10.1	1	5	90	9.8	1.1	3.9	N	63.49	64.86	70	105
32	raghupathy	51	M	father	67	no	no	130/80	125	A	9.8	2	4	140	11.4	0.8	4.1	N	103.52	108.32	103	107
33	mamangam	45	M	father	59	no	no	124/80	180	B	11.9	2	3	124	8.8	0.9	4	N	86.5	96.99	103	119
34	Rani	40	F	sister	53	no	no	110/70	90	O	10.9	3	3	156	13.2	1.2	4.3	N	52.14	52.88	57	82.47
35	dhanalakshmi	50	F	mother	57	no	no	134/90	110	AB	11	2	4	89	11.8	1.1	3.8	N	55.06	55.88	59	93
36	pambavasan	33	M	son	61	no	no	110/80	135	O	13.1	1	2	103	7.4	1	4.1	N	90.65	91.46	98	119
37	rukmani	52	F	mother	63	no	no	140/80	160	O	12	2	6	93	7.9	1	3.9	N	65.45	61.88	65	80.41
38	mayakrishnan	55	M	father	59	no	no	112/80	115	B	9.1	2	4	124	13.9	1.2	4	N	58.04	66.81	68	113
39	Sridevi	27	F	sister	51	no	no	108/70	95	A	11.7	1	5	91	11.1	1.1	4.1	N	61.85	63.33	69	107
40	narkalai	43	F	sister	54	no	no	120/76	140	O	10.3	2	6	165	7.6	0.9	4	N	68.71	72.63	79	101
41	balasubramanian	44	M	brother	58	no	no	130/80	125	O	12.8	3	5	102	11	1.2	3.8	N	64.44	69.91	73	1
42	Muthu	55	M	father	61	no	no	140/90	170	A	11.3	1	7	91	2	1.3	4.3	N	55.4	60.92	67	81.39
43	madheshwari	31	F	sister	57	no	no	110/70	185	O	10.1	3	5	155	13.9	1	3.9	N	73.35	68.73	75	113
44	baskaravalli	55	F	mother	64	no	no	130/80	135	B	9.9	2	4	183	8.9	1.1	4.1	N	58.38	54.81	57	97
45	thiraviyam	54	M	father	67	no	no	116/80	160	O	11.9	1	6	111	9.9	1.2	3.7	N	66.69	67.06	68	93
46	Amutha	45	F	mother	58	no	no	124/82	95	A	10.8	2	3	170	7.4	1	4	N	65.05	63.73	68	122
47	jeyalakshmi	38	F	sister	62	no	no	116/76	175	O	12.4	3	4	134	7.6	0.9	3.8	N	79.7	72.98	79	115
48	ramarajan	29	M	brother	61	no	no	110/80	130	B	13.1	3	4	89	13.2	0.9	4.1	N	104.5	106	115	107
49	manikandan	50	M	father	64	no	no	130/84	108	B	10.7	2	5	161	7.1	0.9	4.2	N	88.89	94.93	98	93
50	chandran	38	M	brother	59	no	no	120/80	165	AB	13.5	1	6	101	15.1	1.1	3.8	N	75.98	79.63	92	113

KEY WORDS FOR MASTER CHART

W t.	- weight in kg
HT/DM	- past history of hypertension and diabetes
F.H/O. RD	- family history of renal disease
BP	- blood pressure
24HR UP	- 24 hour urine protein
Bl.G	- blood group
Hb	- hemoglobin
BT	- bleeding time
CT	- clotting time
BUN	- blood urea nitrogen
S.Cr	- serum creatinine
Alb	- albumin
USG	- ultrasonogram
C-G	- GFR by cockcroft gault formula